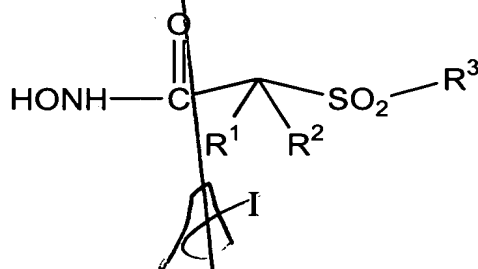


WHAT IS CLAIMED:

1. A process for treating a host mammal having a condition associated with pathological matrix metalloprotease (MMP) activity that comprises administering a metalloprotease inhibitor compound or a pharmaceutically acceptable salt thereof in an effective amount to a mammalian host having such a condition, said metalloprotease inhibitor inhibiting the activity of one or more of MMP-2, MMP-9 and MMP-13, while exhibiting substantially less inhibitory activity against MMP-1, said compound corresponding in structure to formula (I), below



wherein

R¹ and R² are both hydrido or R¹ and R² together with the atoms to which they are bonded form a 5- to 8-membered ring containing one, two or three heteroatoms in the ring that are oxygen, sulfur or nitrogen;

R³ is an optionally substituted aryl or optionally substituted heteroaryl radical, and when said aryl or heteroaryl radical is substituted, the substituent is (a) selected from the group consisting of an optionally substituted cycloalkyl, heterocycloalkyl, aryl, heteroaryl, aralkyl, heteroaralkyl, aralkoxy, heteroaralkoxy, aralkoxyalkyl, aryloxyalkyl, aralkanoylalkyl,

arylcarbonylalkyl, aralkylaryl, aryloxyalkylaryl,
aralkoxyaryl, arylazoaryl, arylhydrazinoaryl,
alkylthioaryl, arylthioalkyl, alkylthioaralkyl,
aralkylthioalkyl, an aralkylthioaryl radical, the
5 sulfoxide or sulfone of any of the thio substituents,
and a fused ring structure comprising two or more 5-
or 6-membered rings selected from the group
consisting of aryl, heteroaryl, cycloalkyl and
heterocycloalkyl, and (b) is itself optionally
10 substituted with one or more substituents
independently selected from the group consisting of a
cyano, perfluoroalkyl, trifluoromethoxy,
trifluoromethylthio, haloalkyl, trifluoromethylalkyl,
aralkoxycarbonyl, aryloxycarbonyl, hydroxy, halo,
15 alkyl, alkoxy, nitro, thiol, hydroxycarbonyl,
aryloxy, arylthio, aralkyl, aryl, arylcarbonylamino,
heteroaryloxy, heteroarylthio, heteroaralkyl,
cycloalkyl, heterocyclooxy, heterocyclothio,
heterocycloamino, cycloalkyloxy, cycloalkylthio,
20 heteroaralkoxy, heteroaralkylthio, aralkoxy,
aralkylthio, aralkylamino, heterocyclo, heteroaryl,
arylazo, hydroxycarbonylalkoxy, alkoxycarbonylalkoxy,
alkanoyl, arylcarbonyl, aralkanoyl, alkanoyloxy,
aralkanoyloxy, hydroxyalkyl, hydroxyalkoxy,
25 alkylthio, alkoxyalkylthio, alkoxycarbonyl,
aryloxyalkoxyaryl, arylthioalkylthioaryl,
aryloxyalkylthioaryl, arylthioalkoxyaryl,
hydroxycarbonylalkoxy, hydroxycarbonylalkylthio,
alkoxycarbonylalkoxy, alkoxycarbonylalkylthio, amino,
30 wherein the amino nitrogen is (i) unsubstituted,
or (ii) substituted with one or two substituents
that are independently selected from the group
consisting of an alkyl, aryl, heteroaryl,

664750-237750

aralkyl, cycloalkyl, aralkoxycarbonyl,
alkoxycarbonyl, arylcarbonyl, aralkanoyl,
heteroarylcarbonyl, heteroaralkanoyl and an
alkanoyl group, or (iii) wherein the amino
5 nitrogen and two substituents attached thereto
form a 5- to 8-membered heterocyclo or
heteroaryl ring containing zero to two
additional heteroatoms that are nitrogen, oxygen
or sulfur and which ring itself is (a)
10 unsubstituted or (b) substituted with one or two
groups independently selected from the group
consisting of an aryl, alkyl, heteroaryl,
aralkyl, heteroaralkyl, hydroxy, alkoxy,
alkanoyl, cycloalkyl, heterocycloalkyl,
15 alkoxycarbonyl, hydroxyalkyl, trifluoromethyl,
benzofused heterocycloalkyl, hydroxyalkoxyalkyl,
aralkoxycarbonyl, hydroxycarbonyl,
aryloxycarbonyl, benzofused heterocycloalkoxy,
benzofused cycloalkylcarbonyl, heterocyclo-
20 alkylcarbonyl, and a cycloalkylcarbonyl group,
carbonylamino

wherein the carbonylamino nitrogen is (i)
unsubstituted, or (ii) is the reacted amine of
an amino acid, or (iii) substituted with one or
25 two radicals selected from the group consisting
of an alkyl, hydroxyalkyl, hydroxyheteroaralkyl,
cycloalkyl, aralkyl, trifluoromethylalkyl,
heterocycloalkyl, benzofused heterocycloalkyl,
benzofused heterocycloalkyl, benzofused
30 cycloalkyl, and an N,N-dialkylsubstituted
alkylamino-alkyl group, or (iv) the carboxamido
nitrogen and two substituents bonded thereto
together form a 5- to 8-membered heterocyclo,

heteroaryl or benzofused heterocycloalkyl ring
that is itself unsubstituted or substituted with
one or two radicals independently selected from
the group consisting of an alkyl,
5 alkoxy carbonyl, nitro, heterocycloalkyl,
hydroxy, hydroxy carbonyl, aryl, aralkyl,
heteroaralkyl and an amino group,

wherein the amino nitrogen is

(i) unsubstituted, or (ii) substituted with
10 one or two substituents that are
independently selected from the group
consisting of alkyl, aryl, and heteroaryl,
or (iii) wherein the amino nitrogen and two
substituents attached thereto form a 5- to
15 8-membered heterocyclo or heteroaryl ring,
and an aminoalkyl group

wherein the aminoalkyl nitrogen is (i)
unsubstituted, or (ii) substituted with one or two
substituents independently selected from the group
20 consisting of an alkyl, aryl, aralkyl, cycloalkyl,
aralkoxy carbonyl, alkoxy carbonyl, and an alkanoyl
group, or (iii) wherein the aminoalkyl nitrogen and
two substituents attached thereto form a 5- to 8-
membered heterocyclo or heteroaryl ring.

25

2. The process according to claim 1
wherein R^1 and R^2 together with the atoms to which
they are bonded form a 5- to 8-membered ring
containing one, two or three heteroatoms in the ring
30 that are oxygen, sulfur or nitrogen;

3. The process according to claim 2
wherein R^3 is a single-ringed aryl or heteroaryl
group that is 5- or 6-membered, and is itself
substituted at its own 4-position when a 6-membered
5 ring or at its own 3- or 4-position when a 5-membered
ring with a substituent selected from the group
consisting of one other single-ringed aryl or
heteroaryl group, a C_3 - C_{14} alkyl group, a N-piperidyl
group, a N-piperazinyl group, a phenoxy group, a
10 thiophenoxy group, a 4-thiopyridyl group, a phenylazo
group and a benzamido group.

4. The process according to claim 3
wherein R^3 contains two or more 5- or 6-membered
15 rings.

5. The process according to claim 3
wherein R^3 , when rotated about an axis drawn through
the SO_2 -bonded 1-position and the substituent-bonded
20 4-position of a 6-membered ring or the SO_2 -bonded 1-
position and substituent-bonded 3- or 4-position of a
5-membered ring, defines a three-dimensional volume
whose widest dimension has the width in a direction
transverse to that axis to rotation of about one
25 furanyl ring to about two phenyl rings.

6. The process according to claim 3
wherein R^3 has a length that is greater than that of
a pentyl group and a length that is less than that of
30 an icosyl group.

[illegible]

wherein

R¹⁴ is hydrido, a pharmaceutically acceptable cation of C(W)R¹⁵ where W is O or S and R¹⁵ is selected from the group consisting of a C₁-C₆-alkyl, aryl, C₁-C₆-alkoxy, heteroaryl-C₁-C₆-alkyl, C₃-C₈-cycloalkyl-C₁-C₆-alkyl, aryloxy, ar-C₁-C₆-alkoxy, ar-C₁-C₆-alkyl, heteroaryl and amino C₁-C₆-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an C₁-C₆-alkyl, aryl, ar-C₁-C₆-alkyl,

C₃-C₈-cycloalkyl-C₁-C₆-alkyl, ar-C₁-C₆-alkoxycarbonyl, C₁-C₆-alkoxycarbonyl, and C₁-C₆-alkanoyl radical, or (iii) wherein the amino C₁-C₆-alkyl nitrogen and two substituents attached thereto
5 form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1 or 2;

n is zero, 1 or 2;

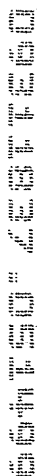
p is zero, 1 or 2;

10 the sum of m + n + p = 1, 2, 3 or 4;

(a) one of X, Y and Z is selected from the group consisting of C(O), NR⁶, O, S, S(O), S(O)₂ and NS(O)₂R⁷, and the remaining two of X, Y and Z are CR⁸R⁹, and CR¹⁰R¹¹, or

15 (b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of NR⁶C(O), NR⁶S(O), NR⁶S(O)₂, NR⁶S, NR⁶O, SS, NR⁶NR⁶ and OC(O), with the remaining one of X, Y and Z being CR⁸R⁹, or

20 (c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of



5 wherein wavy lines are bonds to the atoms
of the depicted ring;

R^6 and $R^{6'}$ are independently selected from the group consisting of hydrido, formyl, sulfonic- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxycarbonyl- C_1 - C_6 -alkyl, hydroxycarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkylcarbonyl- C_1 - C_6 -alkyl, R^8R^9 -aminocarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -

alkoxycarbonyl-C₁-C₆-alkylcarbonyl, hydroxycarbonyl-
C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonyl-C₁-C₆-
alkylcarbonyl, C₁-C₆-alkoxycarbonylcarbonyl,
hydroxycarbonylcarbonyl, C₁-C₆-alkylcarbonylcarbonyl,
5 R⁸R⁹-aminocarbonylcarbonyl, C₁-C₆-alkanoyl, aryl-C₁-
C₆-alkyl, aroyl, bis(C₁-C₆-alkoxy-C₁-C₆-alkyl)-C₁-C₆-
alkyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-
perfluoroalkyl, C₁-C₆-trifluoromethylalkyl, C₁-C₆-
perfluoroalkoxy-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-
10 alkyl, C₃-C₆-cycloalkyl, heteroarycarbonyl,
heterocyclocarbonyl, C₃-C₈-heterocycloalkyl, C₃-C₈-
heterocycloalkylcarbonyl, aryl, C₅-C₆-heterocyclo,
C₅-C₆-heteroaryl, C₃-C₈-cycloalkyl-C₁-C₆-alkyl,
aryloxy-C₁-C₆-alkyl, heteroaryloxy-C₁-C₆-alkyl,
15 heteroaryl-C₁-C₆-alkoxy-C₁-C₆-alkyl, heteroarylthio-
C₁-C₆-alkyl, arylsulfonyl, C₁-C₆-alkylsulfonyl, C₅-
C₆-heteroarylsulfonyl, carboxy-C₁-C₆-alkyl, C₁-C₄-
alkoxycarbonyl-C₁-C₆-alkyl, aminocarbonyl, C₁-C₆-
alkyl(R⁸N)iminocarbonyl, aryl(R⁸N)iminocarbonyl, C₅-
20 C₆-heterocyclo(R⁸N)iminocarbonyl, arylthio-C₁-C₆-
alkyl, C₁-C₆-alkylthio-C₁-C₆-alkyl, arylthio-C₃-C₆-
alkenyl, C₁-C₄-alkylthio-C₃-C₆-alkenyl, C₅-C₆-
heteroaryl-C₁-C₆-alkyl, halo-C₁-C₆-alkanoyl, hydroxy-
C₁-C₆-alkanoyl, thiol-C₁-C₆-alkanoyl, C₃-C₆-alkenyl,
25 C₃-C₆-alkynyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₅-
alkoxycarbonyl, aryloxy carbonyl, NR⁸R⁹-
(R⁸)iminomethyl, NR⁸R⁹-C₁-C₅-alkylcarbonyl, hydroxy-

604730-237660

C₁-C₅-alkyl, R⁸R⁹-aminocarbonyl, R⁸R⁹-aminocarbonyl-
C₁-C₆-alkylcarbonyl, hydroxyaminocarbonyl, R⁸R⁹-
aminosulfonyl, R⁸R⁹-aminosulfon-C₁-C₆-alkyl, R⁸R⁹-
amino-C₁-C₆-alkylsulfonyl and an R⁸R⁹-amino-C₁-C₆-
5 alkyl group;

R⁷ is selected from the group consisting of
a arylalkyl, aryl, heteroaryl, heterocyclo, C₁-C₆-
alkyl, C₃-C₆-alkynyl, C₃-C₆-alkenyl, C₁-C₆-
carboxyalkyl and a C₁-C₆-hydroxyalkyl group;

10 R⁸ and R⁹ and R¹⁰ and R¹¹ are independently
selected from the group consisting of a hydrido,
hydroxy, C₁-C₆-alkyl, C₁-C₆-alkanoyl, aroyl, aryl,
ar-C₁-C₆-alkyl, heteroaryl, heteroar-C₁-C₆-alkyl, C₂-
C₆-alkynyl, C₂-C₆-alkenyl, thiol-C₁-C₆-alkyl, C₁-C₆-
15 alkylthio-C₁-C₆-alkyl, cycloalkyl, cycloalkyl-C₁-C₆-
alkyl, heterocycloalkyl-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-
C₆-alkyl, aralkoxy-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-
alkoxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl,
hydroxycarbonyl-C₁-C₆-alkyl, hydroxycarbonylar-C₁-C₆-
20 alkyl, aminocarbonyl-C₁-C₆-alkyl, aryloxy-C₁-C₆-
alkyl, heteroaryloxy-C₁-C₆-alkyl, arylthio-C₁-C₆-
alkyl, heteroarylthio-C₁-C₆-alkyl, the sulfoxide or
sulfone of any said thio substituents, perfluoro-C₁-
C₆-alkyl, trifluoromethyl-C₁-C₆-alkyl, halo-C₁-C₆-
25 alkyl, alkoxycarbonylamino-C₁-C₆-alkyl and an amino-
C₁-C₆-alkyl group wherein the aminoalkyl nitrogen is
(i) unsubstituted or (ii) substituted with one or two

radicals independently selected from the group consisting of C₁-C₆-alkyl, ar-C₁-C₆-alkyl, cycloalkyl and C₁-C₆-alkanoyl, or wherein R⁸ and R⁹ or R¹⁰ and R¹¹ and the carbon to which they are bonded form a carbonyl group, or wherein R⁸ and R⁹ or R¹⁰ and R¹¹, or R⁸ and R¹⁰ together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen, oxygen, or sulfur, with the proviso that only one of R⁸ and R⁹ or R¹⁰ and R¹¹ is hydroxy;

R¹² and R^{12'} are independently selected from the group consisting of a hydrido, C₁-C₆-alkyl, aryl, ar-C₁-C₆-alkyl, heteroaryl, heteroaralkyl, C₂-C₆-alkynyl, C₂-C₆-alkenyl, thiol-C₁-C₆-alkyl, cycloalkyl, cycloalkyl-C₁-C₆-alkyl, heterocycloalkyl-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkoxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl, hydroxycarbonyl-C₁-C₆-alkyl, hydroxycarbonylar-C₁-C₆-alkyl, aminocarbonyl-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, heteroaryloxy-C₁-C₆-alkyl, C₁-C₆-alkylthio-C₁-C₆-alkyl, arylthio-C₁-C₆-alkyl, heteroarylthio-C₁-C₆-alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro-C₁-C₆-alkyl, trifluoromethyl-C₁-C₆-alkyl, halo-C₁-C₆-alkyl, alkoxycarbonylamino-C₁-C₆-alkyl and an amino-C₁-C₆-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii)

substituted with one or two radicals independently selected from the group consisting of C_1-C_6 -alkyl, ar- C_1-C_6 -alkyl, cycloalkyl and C_1-C_6 -alkanoyl;

R^{13} is selected from the group consisting of a hydrido, benzyl, phenyl, C_1-C_6 -alkyl, C_2-C_6 -alkynyl, C_2-C_6 -alkenyl and a C_1-C_6 -hydroxyalkyl group; and

G-A-R-E-Y is a substituent that has a length greater than that of a pentyl group has a length that is less than that of an icosyl group wherein

G is an aryl or heteroaryl group;

A is selected from the group consisting of

- (1) -O-;
- (2) -S-;
- (3) -NR¹⁷-;
- (4) -CO-N(R¹⁷) or -N(R¹⁷)-CO-, wherein R¹⁷ is hydrogen, C_1-C_4 -alkyl, or phenyl;
- (5) -CO-O- or -O-CO-;
- (6) -O-CO-O-;
- (7) -HC=CH-;
- (8) -NH-CO-NH-;
- (9) -C≡C-;
- (10) -NH-CO-O- or -O-CO-NH-;
- (11) -N=N-;
- (12) -NH-NH-; and
- (13) -CS-N(R¹⁸)- or -N(R¹⁸)-CS-, wherein R¹⁸ is hydrogen C_1-C_4 -alkyl, or phenyl; or

(14) A is absent and G is bonded directly to R;

R is a moiety selected from the group consisting of alkyl, alkoxyalkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroaralkyl, heterocycloalkylalkyl, cycloalkylalkyl, cycloalkoxyalkyl, heterocycloalkoxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, arylthioalkyl, heteroarylthioalkyl, cycloalkylthioalkyl, and a heterocycloalkylthioalkyl group wherein the aryl or heteroaryl or cycloalkyl or heterocycloalkyl substituent is (i) unsubstituted or (ii) substituted with one or two radicals selected from the group consisting of a halo, alkyl, perfluoroalkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, amino, alkoxycarbonylalkyl, alkoxy, C₁-C₂-alkylene-dioxy, hydroxycarbonylalkyl, hydroxycarbonylalkylamino, nitro, hydroxy, hydroxyalkyl, alkanoylamino, and a alkoxycarbonyl group, and R is other than alkyl or alkoxyalkyl when A is -O- or -S-;

E is selected from the group consisting of

- (1) -CO(R¹⁹)- or -(R¹⁹)CO-, wherein R¹⁹ is a heterocycloalkyl, or a cycloalkyl group;
- (2) -CONH- or -HNCO-; and
- (3) -CO-;
- (4) -SO₂-R¹⁹- or -R¹⁹-SO₂-;
- (5) -SO₂-;
- (6) -NH-SO₂- or -SO₂-NH-; or

(7) E is absent and R is bonded directly to Y; and

Y is absent or is selected from the group consisting of a hydrido, alkyl, alkoxy, haloalkyl, aryl, aralkyl, cycloalkyl, heteroaryl, hydroxy, aryloxy, aralkoxy, heteroaryloxy, heteroaralkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, alkenyl, heterocycloalkyl, cycloalkyl, trifluoromethyl, alkoxycarbonyl, and a aminoalkyl group, wherein the aryl or heteroaryl or heterocycloalkyl group is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of an alkanoyl, halo, nitro, aralkyl, aryl, alkoxy, and an amino group wherein the amino nitrogen is (i) unsubstituted or (ii) substituted with one or two groups independently selected from hydrido, alkyl, and an aralkyl group.

Sub 20
B5

~~8. The process according to claim 7 wherein said -G-A-R-E-Y substituent contains two to four carbocyclic or heterocyclic rings.~~

9. The process according to claim 8 wherein each of the two to four rings is 6-membered.

10. The process according to claim 7 wherein said -G-A-R-E-Y substituent has a length that is greater than a hexyl group and a length that is less than that of a stearyl group.

Sub
B6

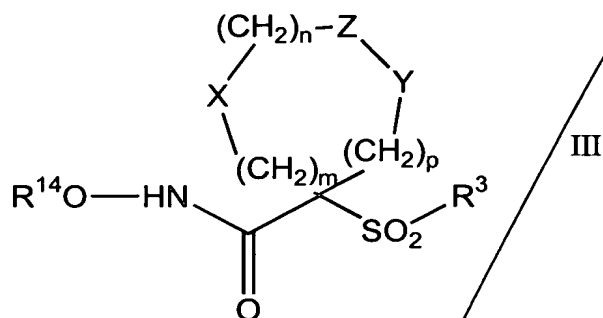
5

10

Sub
B77

15

15. A process for treating a host mammal having a condition associated with pathological matrix metalloprotease (MMP) activity that comprises administering a metalloprotease inhibitor compound or a pharmaceutically acceptable salt thereof in an effective amount to a mammalian host having such a condition, said metalloprotease inhibitor inhibiting the activity of one or more of MMP-2, MMP-9 and MMP-13, while exhibiting substantially less inhibitory activity against MMP-1, said compound corresponding in structure to formula III, below



wherein

R^3 is a single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself substituted at its own 4-position when a 6-membered ring and at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of a thiophenoxy, 4-chloro-phenoxy, 3-chlorophenoxy, 4-methoxyphenoxy, 3-benzodioxol-5-yloxy, 3,4-dimethylphenoxy, 4-fluorophenoxy, 4-fluorothiophenoxy, phenoxy, 4-trifluoromethoxyphenoxy, 4-trifluoromethylphenoxy, 4-(trifluoromethylthio)phenoxy, 4-(trifluoromethylthio)thiophenoxy, 4-chloro-3-fluorophenoxy, 4-isopropoxyphenoxy, 4-isopropylphenoxy, (2-methyl-1,3-benzothiazol-5-yl)oxy, 4-(1H-imidazol-1-yl)phenoxy, 4-chloro-3-methylphenoxy, 3-methyl-phenoxy, 4-ethoxyphenoxy, 3,4-difluorophenoxy, 4-chloro-3-methylphenoxy, 4-fluoro-3-chlorophenoxy, 4-(1H-1,2,4-triazol-1-yl)phenoxy, 3,5-difluorophenoxy, 3,4-dichlorophenoxy, 4-cyclopentylphenoxy, 4-bromo-3-methylphenoxy, 4-bromophenoxy, 4-methylthiophenoxy, 4-phenylphenoxy, 4-benzylphenoxy, 6-quinolinyloxy, 4-amino-3-methylphenoxy, 3-methoxyphenoxy, 5,6,7,8-tetrahydro-2-naphthalenyloxy, 3-hydroxymethylphenoxy, and a 4-benzyloxyphenoxy group;

5 R^{14} is hydrido, a pharmaceutically acceptable cation or $C(W)R^{15}$ where W is O or S and R^{15} is selected from the group consisting of a C_1 - C_6 -alkyl, aryl, C_1 - C_6 -alkoxy, heteroaryl- C_1 - C_6 -alkyl, C_3 - C_8 -cycloalkyl- C_1 - C_6 -alkyl, aryloxy, ar- C_1 - C_6 -alkoxy, ar- C_1 - C_6 -alkyl, heteroaryl and amino C_1 - C_6 -alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an C_1 - C_6 -alkyl, aryl, ar- C_1 - C_6 -alkyl, C_3 - C_8 -cycloalkyl- C_1 - C_6 -alkyl, ar- C_1 - C_6 -alkoxycarbonyl, C_1 - C_6 -alkoxycarbonyl, and C_1 - C_6 -alkanoyl radical, or (iii) wherein the amino C_1 - C_6 -alkyl nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1 or 2;

n is zero, 1 or 2;

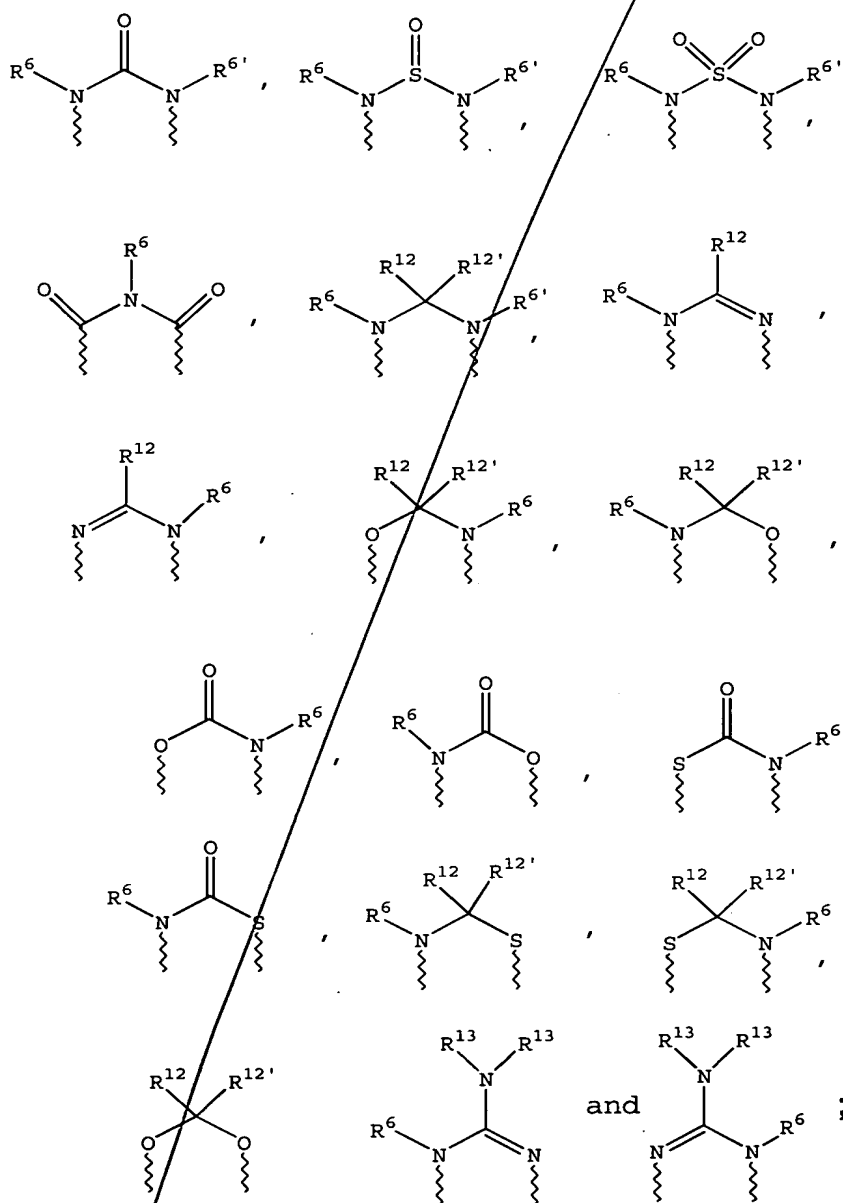
p is zero, 1 or 2;

20 the sum of $m + n + p = 1, 2, 3$ or 4;

(a) one of X, Y and Z is selected from the group consisting of $C(O)$, NR^6 , O, S, $S(O)$, $S(O)_2$ and $NS(O)_2R^7$, and the remaining two of X, Y and Z are CR^8R^9 , and $CR^{10}R^{11}$, or

25 (b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of $NR^6C(O)$, $NR^6S(O)$, $NR^6S(O)_2$, NR^6S , NR^6O , SS , NR^6NR^6 and $OC(O)$, with the remaining one of X, Y and Z being CR^8R^9 , or

(c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of



wherein wavy lines are bonds to the atoms
10 of the depicted ring;

R^6 and $R^{6'}$ are independently selected from the group consisting of hydrido, formyl, sulfonic- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxycarbonyl- C_1 - C_6 -alkyl, hydroxycarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkylcarbonyl- C_1 - C_6 -alkyl, R^8R^9 -aminocarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxycarbonyl- C_1 - C_6 -alkylcarbonyl, hydroxycarbonyl- C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -alkylcarbonyl- C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -alkoxycarbonylcarbonyl, hydroxycarbonylcarbonyl, C_1 - C_6 -alkylcarbonylcarbonyl, R^8R^9 -aminocarbonylcarbonyl, C_1 - C_6 -alkanoyl, aryl- C_1 - C_6 -alkyl, aroyl, bis(C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl)- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_1 - C_6 -perfluoroalkyl, C_1 - C_6 -trifluoromethylalkyl, C_1 - C_6 -perfluoroalkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, heteroarycarbonyl, heterocyclocarbonyl, C_3 - C_8 -heterocycloalkyl, C_3 - C_8 -heterocycloalkylcarbonyl, aryl, C_5 - C_6 -heterocyclo, C_5 - C_6 -heteroaryl, C_3 - C_8 -cycloalkyl- C_1 - C_6 -alkyl, aryloxy- C_1 - C_6 -alkyl, heteroaryloxy- C_1 - C_6 -alkyl, heteroaryl- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, heteroarylthio- C_1 - C_6 -alkyl, arylsulfonyl, C_1 - C_6 -alkylsulfonyl, C_5 - C_6 -heteroarylsulfonyl, carboxy- C_1 - C_6 -alkyl, C_1 - C_4 -alkoxycarbonyl- C_1 - C_6 -alkyl, aminocarbonyl, C_1 - C_6 -alkyl(R^8N)iminocarbonyl, aryl(R^8N)iminocarbonyl, C_5 - C_6 -heterocyclo(R^8N)iminocarbonyl, arylthio- C_1 - C_6 -alkyl, C_1 - C_6 -alkylthio- C_1 - C_6 -alkyl, arylthio- C_3 - C_6 -alkenyl, C_1 - C_4 -alkylthio- C_3 - C_6 -alkenyl, C_5 - C_6 -

heteroaryl-C₁-C₆-alkyl, halo-C₁-C₆-alkanoyl, hydroxy-C₁-C₆-alkanoyl, thiol-C₁-C₆-alkanoyl, C₃-C₆-alkenyl, C₃-C₆-alkynyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₅-alkoxycarbonyl, aryloxycarbonyl, NR⁸R⁹-

- 5 (R⁸)iminomethyl, NR⁸R⁹-C₁-C₅-alkylcarbonyl, hydroxy-C₁-C₅-alkyl, R⁸R⁹-aminocarbonyl, R⁸R⁹-aminocarbonyl-C₁-C₆-alkylcarbonyl, hydroxyaminocarbonyl, R⁸R⁹-aminosulfonyl, R⁸R⁹-aminosulfon-C₁-C₆-alkyl, R⁸R⁹-amino-C₁-C₆-alkylsulfonyl and an R⁸R⁹-amino-C₁-C₆-alkyl group;
- 10

R⁷ is selected from the group consisting of a arylalkyl, aryl, heteroaryl, heterocyclo, C₁-C₆-alkyl, C₃-C₆-alkynyl, C₃-C₆-alkenyl, C₁-C₆-carboxyalkyl and a C₁-C₆-hydroxyalkyl group;

- 15 R⁸ and R⁹ and R¹⁰ and R¹¹ are independently selected from the group consisting of a hydrido, hydroxy, C₁-C₆-alkyl, C₁-C₆-alkanoyl, aroyl, aryl, ar-C₁-C₆-alkyl, heteroaryl, heteroar-C₁-C₆-alkyl, C₂-C₆-alkynyl, C₂-C₆-alkenyl, thiol-C₁-C₆-alkyl, C₁-C₆-alkylthio-C₁-C₆-alkyl, cycloalkyl, cycloalkyl-C₁-C₆-alkyl, heterocycloalkyl-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, aralkoxy-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkoxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl, hydroxycarbonyl-C₁-C₆-alkyl, hydroxycarbonylar-C₁-C₆-alkyl, aminocarbonyl-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, heteroaryloxy-C₁-C₆-alkyl, arylthio-C₁-C₆-alkyl, heteroarylthio-C₁-C₆-alkyl, the sulfoxide or
- 20
- 25

66450-25450

sulfone of any said thio substituents, perfluoro-C₁-C₆-alkyl, trifluoromethyl-C₁-C₆-alkyl, halo-C₁-C₆-alkyl, alkoxycarbonylamino-C₁-C₆-alkyl and an amino-C₁-C₆-alkyl group wherein the aminoalkyl nitrogen is

5 (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C₁-C₆-alkyl, ar-C₁-C₆-alkyl, cycloalkyl and C₁-C₆-alkanoyl, or wherein R⁸ and R⁹ or R¹⁰ and R¹¹ and the carbon to which they are bonded form a

10 carbonyl group, or wherein R⁸ and R⁹ or R¹⁰ and R¹¹, or R⁸ and R¹⁰ together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen,

15 oxygen, or sulfur, with the proviso that only one of R⁸ and R⁹ or R¹⁰ and R¹¹ is hydroxy;

R¹² and R^{12'} are independently selected from the group consisting of a hydrido, C₁-C₆-alkyl, aryl, ar-C₁-C₆-alkyl, heteroaryl, heteroaralkyl, C₂-C₆-alkynyl, C₂-C₆-alkenyl, thiol-C₁-C₆-alkyl,

20 cycloalkyl, cycloalkyl-C₁-C₆-alkyl, heterocycloalkyl-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkoxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl, hydroxycarbonyl-C₁-C₆-alkyl, hydroxycarbonylar-C₁-C₆-alkyl,

25 aminocarbonyl-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, heteroaryloxy-C₁-C₆-alkyl, C₁-C₆-alkylthio-C₁-C₆-alkyl, arylthio-C₁-C₆-alkyl, heteroarylthio-C₁-C₆-

alkyl, the sulfoxide or sulfone of any said thio
substituents, perfluoro-C₁-C₆-alkyl, trifluoromethyl-
C₁-C₆-alkyl, halo-C₁-C₆-alkyl, alkoxycarbonylamino-
C₁-C₆-alkyl and an amino-C₁-C₆-alkyl group wherein
5 the aminoalkyl nitrogen is (i) unsubstituted or (ii)
substituted with one or two radicals independently
selected from the group consisting of C₁-C₆-alkyl,
ar-C₁-C₆-alkyl, cycloalkyl and C₁-C₆-alkanoyl; and

R¹³ is selected from the group consisting
10 of a hydrido, benzyl, phenyl, C₁-C₆-alkyl, C₂-C₆-
alkynyl, C₂-C₆-alkenyl and a C₁-C₆-hydroxyalkyl
group.

16. The process according to claim 15
15 ~~wherein the sum of m + n + p = 1 or 2.~~

~~17. The process according to claim 15
wherein Z is O, S or NR⁶.~~

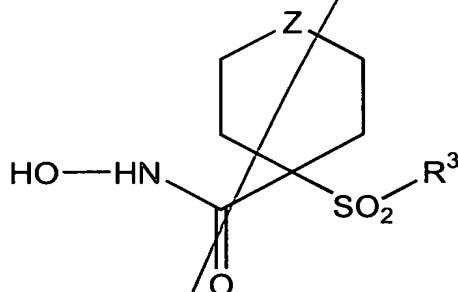
20 18. The process according to claim 15
wherein R⁶ is selected from the group consisting of
C₃-C₆-cycloalkyl, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-
alkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl,
aminosulfonyl, heteroaryl-C₁-C₆-alkyl,
25 aryloxycarbonyl, and C₁-C₆-alkoxycarbonyl.

19. The process according to claim 15
wherein m = n = zero, p = 1, and Y is NR⁶.

001150 423760

Sub B9

20. ~~A process for treating a host mammal~~
 having a condition associated with pathological
 matrix metalloprotease (MMP) activity that comprises
 administering a metalloprotease inhibitor compound or
 5 a pharmaceutically acceptable salt thereof in an
 effective amount to a mammalian host having such a
 condition, said metalloprotease inhibitor inhibiting
 the activity of one or more of MMP-2, MMP-9 and MMP-
 13, while exhibiting substantially less inhibitory
 10 activity against MMP-1, said compound corresponding
 in structure to formula IV, below



IV

wherein R^3 is an optionally substituted
 15 aryl or optionally substituted heteroaryl radical,
 and when said aryl or heteroaryl radical is
 substituted, the substituent is (a) selected from the
 group consisting of an optionally substituted
 cycloalkyl, heterocycloalkyl, aryl, heteroaryl,
 20 aralkyl, heteroaralkyl, aralkoxy, heteroaralkoxy,
 aralkoxyalkyl, aryloxyalkyl, aralkanoylalkyl,
 arylcarbonylalkyl, aralkylaryl, aryloxyalkylaryl,
 aralkoxyaryl, arylazoaryl, arylhydrazinoaryl,
 alkylthioaryl, arylthioalkyl, alkylthioaralkyl,
 25 aralkylthioalkyl, an aralkylthioaryl radical, the
 sulfoxide or sulfone of any of the thio substituents,
 and a fused ring structure comprising two or more 5-

004450 484660

or 6-membered rings selected from the group consisting of aryl, heteroaryl, cycloalkyl and heterocycloalkyl, and (b) is itself optionally substituted with one or more substituents

5 independently selected from the group consisting of a cyano, perfluoroalkyl, trifluoromethoxy, trifluoromethylthio, haloalkyl, trifluoromethylalkyl, aralkoxycarbonyl, aryloxycarbonyl, hydroxy, halo, alkyl, alkoxy, nitro, thiol, hydroxycarbonyl,

10 aryloxy, arylthio, aralkyl, aryl, arylcarbonylamino, heteroaryloxy, heteroarylthio, heteroaralkyl, cycloalkyl, heterocyclooxy, heterocyclothio, heterocycloamino, cycloalkyloxy, cycloalkylthio, heteroaralkoxy, heteroaralkylthio, aralkoxy,

15 aralkylthio, aralkylamino, heterocyclo, heteroaryl, arylazo, hydroxycarbonylalkoxy, alkoxycarbonylalkoxy, alkanoyl, arylcarbonyl, aralkanoyl, alkanoyloxy, aralkanoyloxy, hydroxyalkyl, hydroxyalkoxy, alkylthio, alkoxyalkylthio, alkoxycarbonyl,

20 aryloxyalkoxyaryl, arylthioalkylthioaryl, aryloxyalkylthioaryl, arylthioalkoxyaryl, hydroxycarbonylalkoxy, hydroxycarbonylalkylthio, alkoxycarbonylalkoxy, alkoxycarbonylalkylthio, amino,

25 wherein the amino nitrogen is (i) unsubstituted, or (ii) substituted with one or two substituents that are independently selected from the group consisting of an alkyl, aryl, heteroaryl, aralkyl, cycloalkyl, aralkoxycarbonyl, alkoxycarbonyl, arylcarbonyl, aralkanoyl, heteroarylcarbonyl, heteroaralkanoyl and an

30 alkanoyl group, or (iii) wherein the amino nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclo or

0044250

30

hydroxy, hydroxycarbonyl, aryl, aralkyl,
heteroaralkyl and an amino group,

wherein the amino nitrogen is

(i) unsubstituted, or (ii) substituted with
one or two substituents that are
independently selected from the group
consisting of alkyl, aryl, and heteroaryl,
or (iii) wherein the amino nitrogen and two
substituents attached thereto form a 5- to
8-membered heterocyclo or heteroaryl ring,
and an aminoalkyl group

wherein the aminoalkyl nitrogen is (i)
unsubstituted, or (ii) substituted with one or two
substituents independently selected from the group
consisting of an alkyl, aryl, aralkyl, cycloalkyl,
aralkoxycarbonyl, alkoxycarbonyl, and an alkanoyl
group, or (iii) wherein the aminoalkyl nitrogen and
two substituents attached thereto form a 5- to 8-
membered heterocyclo or heteroaryl ring; and

Z is selected group the group consisting of
O, S, NR^6 , SO, SO_2 , and NSO_2R^7 ,

wherein R^6 is selected from the group
consisting of hydrido, $\text{C}_1\text{-C}_5\text{-alkyl}$, $\text{C}_1\text{-C}_5\text{-alkanoyl}$,
benzyl, benzoyl, $\text{C}_3\text{-C}_5\text{-alkynyl}$, $\text{C}_3\text{-C}_5\text{-alkenyl}$, $\text{C}_1\text{-C}_3\text{-}$
 $\text{alkoxy-C}_1\text{-C}_4\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-cycloalkyl}$, heteroaryl- $\text{C}_1\text{-}$
 $\text{C}_6\text{-alkyl}$, $\text{C}_1\text{-C}_5\text{-hydroxyalkyl}$, $\text{C}_1\text{-C}_5\text{-carboxyalkyl}$, $\text{C}_1\text{-}$
 $\text{C}_5\text{-alkoxy C}_1\text{-C}_5\text{-alkylcarbonyl}$, and $\text{NR}^8\text{R}^9\text{-C}_1\text{-C}_5\text{-}$
 alkylcarbonyl or $\text{NR}^8\text{R}^9\text{-C}_1\text{-C}_5\text{-alkyl}$ wherein R^8 and R^9
are independently hydrido, $\text{C}_1\text{-C}_5\text{-alkyl}$, $\text{C}_1\text{-C}_5\text{-}$

alkoxycarbonyl or aryl-C₁-C₅-alkoxycarbonyl, or NR⁸R⁹ together form a heterocyclic ring containing 5- to 8-atoms in the ring; and

R⁷ is selected from the group consisting of
5 a arylalkyl, aryl, heteroaryl, heterocyclo, C₁-C₆-alkyl, C₃-C₆-alkynyl, C₃-C₆-alkenyl, C₁-C₆-carboxyalkyl and a C₁-C₆-hydroxyalkyl group.

21. The process according to claim 20
10 wherein R³ is a single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself substituted at its own 4-position when a 6-membered ring or at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group
15 consisting of one other single-ringed aryl or heteroaryl group, a C₃-C₁₄ alkyl group, a N-piperidyl group, a N-piperazinyl group, a phenoxy group, a thiophenoxy group, a 4-thiopyridyl group, a phenylazo group and a benzamido group.

22. The process according to claim 20
wherein R³ has a length that is greater than that of a pentyl group and a length that is less than that of an icosyl group.

~~23. The process according to claim 20~~
wherein Z is O, S or NR⁶.

24. The process according to claim 23
30 wherein R⁶ is selected from the group consisting of

664T33 423T650

C₃-C₆-cycloalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkynyl, amino-C₁-C₆-alkyl, aminosulfonyl, heteroaryl-C₁-C₆-alkyl, aryloxycarbonyl, and C₁-C₆-alkoxycarbonyl.

5

25. The process according to claim 20 wherein said R³ radical is the substituent G-A-R-E-Y, wherein G is an aryl or heteroaryl group;

A is selected from the group consisting of

10

(1) -O-;

(2) -S-;

(3) -NR¹⁷-;

(4) -CO-N(R¹⁷) or -N(R¹⁷)-CO-, wherein R¹⁷ is hydrogen, C₁-C₄-alkyl, or phenyl;

15

(5) -CO-O- or -O-CO-;

(6) -O-CO-O-;

(7) -HC=CH-;

(8) -NH-CO-NH-;

(9) -C≡C-;

20

(10) -NH-CO-O- or -O-CO-NH-;

(11) -N=N-;

(12) -NH-NH-; and

(13) -CS-N(R¹⁸)- or -N(R¹⁸)-CS-, wherein R¹⁸ is hydrogen C₁-C₄-alkyl, or

25

phenyl; or

(14) A is absent and G is bonded directly to R;

R is a moiety selected from the group consisting of alkyl, alkoxyalkyl, aryl, heteroaryl,

604730-463760

cycloalkyl, heterocycloalkyl, aralkyl, heteroaralkyl,
heterocycloalkylalkyl, cycloalkylalkyl,
cycloalkoxyalkyl, heterocycloalkoxyalkyl,
aryloxyalkyl, heteroaryloxyalkyl, arylthioalkyl,
5 heteroarylthioalkyl, cycloalkylthioalkyl, and a
heterocycloalkylthioalkyl group wherein the aryl or
heteroaryl or cycloalkyl or heterocycloalkyl
substituent is (i) unsubstituted or (ii) substituted
with one or two radicals selected from the group
10 consisting of a halo, alkyl, perfluoroalkyl,
perfluoroalkoxy, perfluoroalkylthio,
trifluoromethylalkyl, amino, alkoxycarbonylalkyl,
alkoxy, C₁-C₂-alkylene-dioxy, hydroxycarbonylalkyl,
hydroxycarbonylalkylamino, nitro, hydroxy,
15 hydroxyalkyl, alkanoylamino, and a alkoxycarbonyl
group, and R is other than alkyl or alkoxyalkyl when
A is -O- or -S-;

E is selected from the group consisting of

- (1) -CO(R¹⁹)- or -(R¹⁹)CO-, wherein R¹⁹ is
20 a heterocycloalkyl, or a cycloalkyl
group;
(2) -CONH- or -HNCO-; and
(3) -CO-;
(4) -SO₂-R¹⁹- or -R¹⁹-SO₂-;
25 (5) -SO₂-;
(6) -NH-SO₂- or -SO₂-NH-; or
(7) E is absent and R is bonded directly
to Y; and

Y is absent or is selected from the group
30 consisting of a hydrido, alkyl, alkoxy, haloalkyl,

aryl, aralkyl, cycloalkyl, heteroaryl, hydroxy,
aryloxy, aralkoxy, heteroaryloxy, heteroaralkyl,
perfluoroalkoxy, perfluoroalkylthio,
trifluoromethylalkyl, alkenyl, heterocycloalkyl,
5 cycloalkyl, trifluoromethyl, alkoxycarbonyl, and a
aminoalkyl group, wherein the aryl or heteroaryl or
heterocycloalkyl group is (i) unsubstituted or (ii)
substituted with one or two radicals independently
selected from the group consisting of an alkanoyl,
10 halo, nitro, aralkyl, aryl, alkoxy, and an amino
group wherein the amino nitrogen is (i) unsubstituted
or (ii) substituted with one or two groups
independently selected from hydrido, alkyl, and an
aralkyl group.

15

Set p10
~~26. The process according to claim 25~~
wherein said -G-A-R-E-Y substituent contains two to
four carbocyclic or heterocyclic rings.

20

27. The process according to claim 26
wherein each of the two to four rings is 6-membered.

25

28. The process according to claim 25
wherein said -G-A-R-E-Y substituent has a length that
is greater than a hexyl group and a length that is
~~less than that of a stearyl group.~~

30

29. The process according to claim 25
wherein A is -O- or -S-

30. The process according to claim 25 wherein R is an aryl, heteroaryl, cycloalkyl or heterocycloalkyl group.

5 31. The process according to claim 25 wherein E is absent.

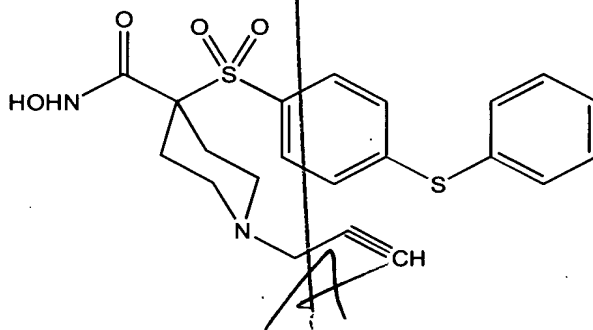
32. The process according to claim 25 wherein Y is selected from the group consisting of
10 hydrido, an alkyl, alkoxy, perfluoroalkoxy and a perfluoroalkylthio group.

33. The process according to claim 20 wherein R³ is a radical that is comprised of a
15 single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself substituted at its own 4-position when a 6-membered ring and at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of a thiophenoxy,
20 4-chlorophenoxy, 3-chlorophenoxy, 4-methoxyphenoxy, 3-benzodioxol-5-yloxy, 3,4-dimethylphenoxy, 4-fluorophenoxy, 4-fluorothiophenoxy, phenoxy, 4-trifluoromethoxy-phenoxy, 4-trifluoromethylphenoxy, 4-(trifluoromethylthio)-phenoxy, 4-
25 (trifluoromethylthio)-thiophenoxy, 4-chloro-3-fluorophenoxy, 4-isopropoxyphenoxy, 4-isopropylphenoxy, (2-methyl-1,3-benzothiazol-5-yl)oxy, 4-(1H-imidazol-1-yl)phenoxy, 4-chloro-3-methylphenoxy, 3-methylphenoxy, 4-ethoxyphenoxy, 3,4-
30 difluorophenoxy, 4-chloro-3-methylphenoxy, 4-fluoro-3-chlorophenoxy, 4-(1H-1,2,4-triazol-1-yl)phenoxy, 3,5-difluorophenoxy, 3,4-dichlorophenoxy, 4-

604730-4-2-1-60

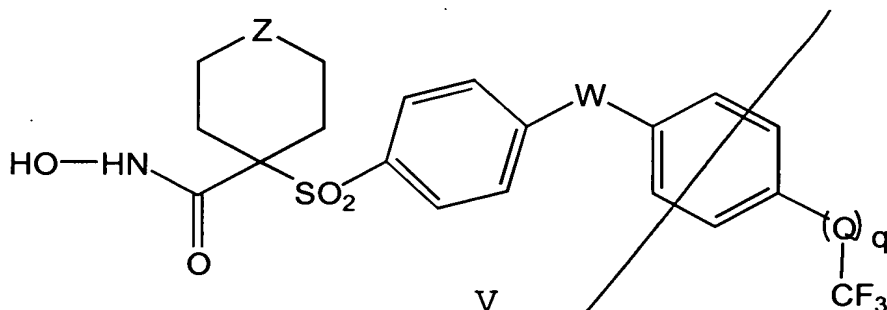
cyclopentylphenoxy, 4-bromo-3-methylphenoxy, 4-bromophenoxy, 4-methylthiophenoxy, 4-phenylphenoxy, 4-benzylphenoxy, 6-quinolinyloxy, 4-amino-3-methylphenoxy, 3-methoxyphenoxy, 5,6,7,8-tetrahydro-
5 2-naphthalenyloxy, 3-hydroxymethylphenoxy, N-piperidyl, N-piperazinyl and a 4-benzyloxyphenoxy group.

34. The process according to claim 20
10 wherein said inhibitor corresponds in structure to the formula



35. A process for treating a host mammal
15 having a condition associated with pathological matrix metalloprotease (MMP) activity that comprises administering a metalloprotease inhibitor compound or a pharmaceutically acceptable salt thereof in an effective amount to a mammalian host having such a
20 condition, said metalloprotease inhibitor inhibiting the activity of one or more of MMP-2, MMP-9 and MMP-13, while exhibiting substantially less inhibitory activity against MMP-1, said compound corresponding in structure to formula V, below

25



wherein

Z is O, S or NR⁶;

5 W and Q are independently oxygen (O), NR⁶ or sulfur (S),

R⁶ is selected from the group consisting of C₃-C₆-cycloalkyl, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, 10 aminosulfonyl, heteroaryl-C₁-C₆-alkyl, aryloxycarbonyl, and C₁-C₆-alkoxycarbonyl; and

q is zero or one such that when q is zero, Q is absent and the trifluoromethyl group is bonded directly to the depicted phenyl ring.

15

36. The process according to claim 35 wherein q is zero.

37. The process according to claim 35 20 wherein W is O.

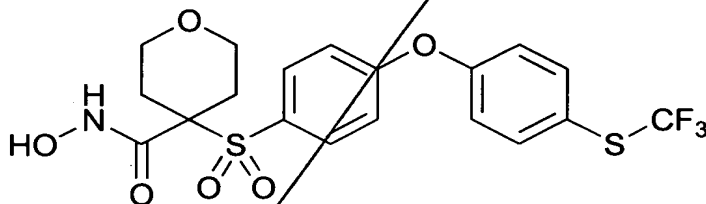
38. The process according to claim 37 wherein q is zero.

39. The process according to claim 37 25 wherein q is one and Q is O.

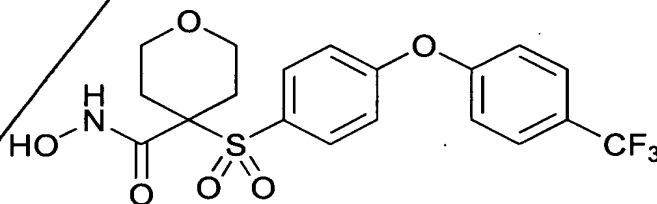
604750 7/28/76

40. The process according to claim 37 wherein q is one and Q is S.

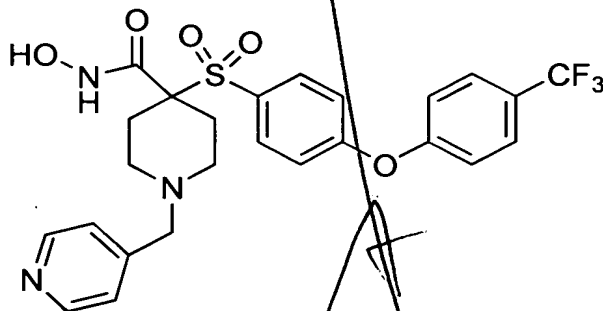
B12 5 ~~41. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula~~



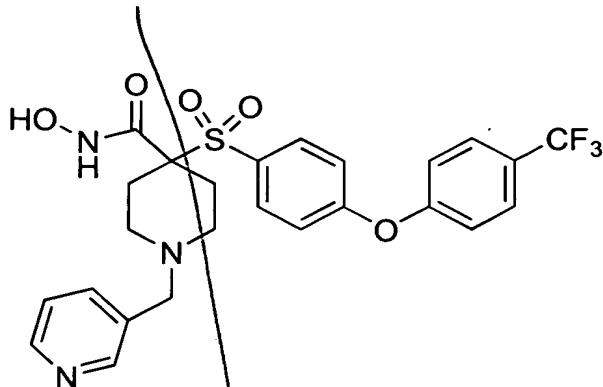
42. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula



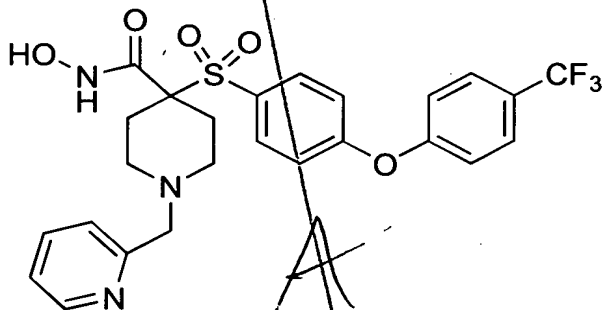
43. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula



44. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula

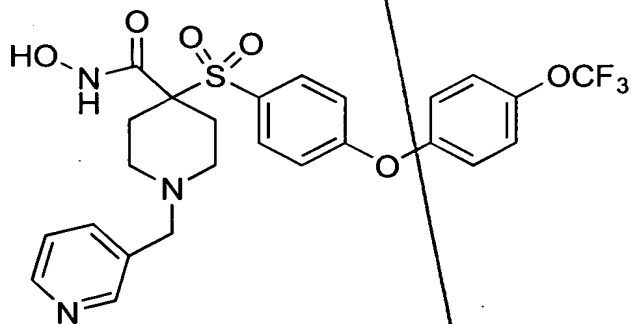


45. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula



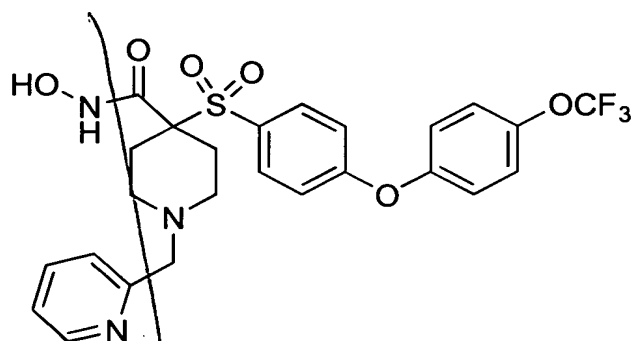
5

46. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula

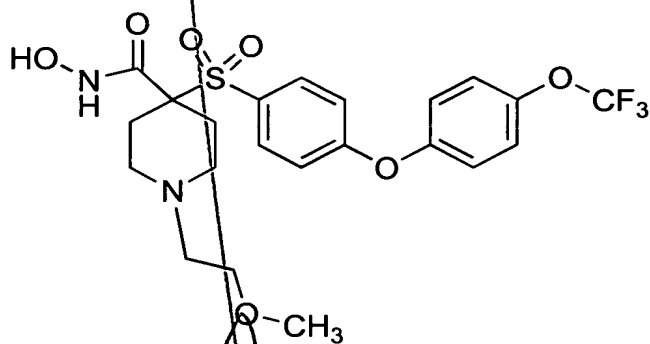


10

47. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula

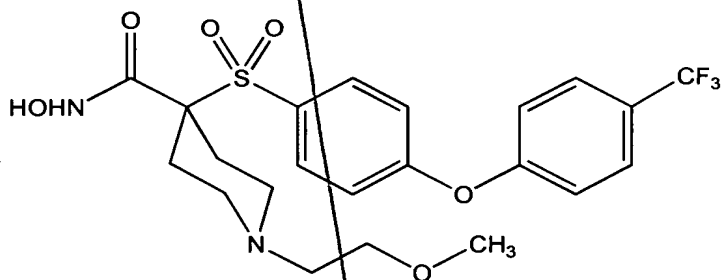


48. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula



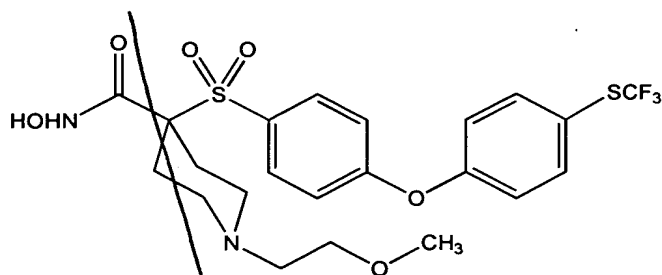
5

49. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula

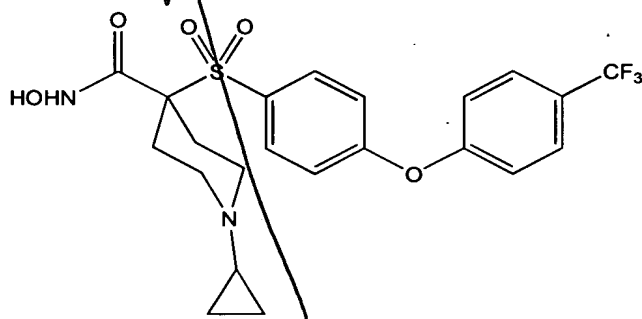


10

50. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula

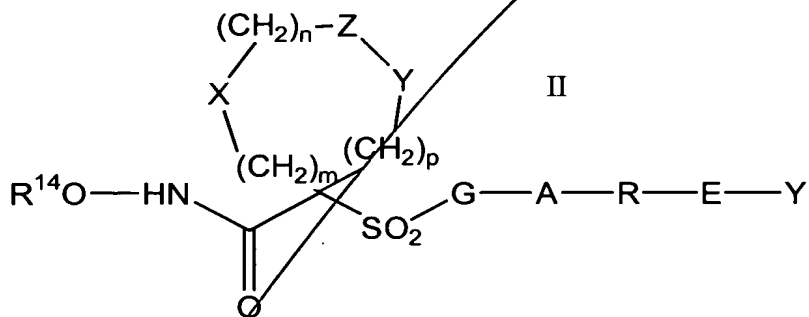


51. The process according to claim 35 wherein said inhibitor corresponds in structure to the formula



5

52. A compound corresponding in structure to formula II, below, or a pharmaceutically acceptable salt thereof:



10

wherein

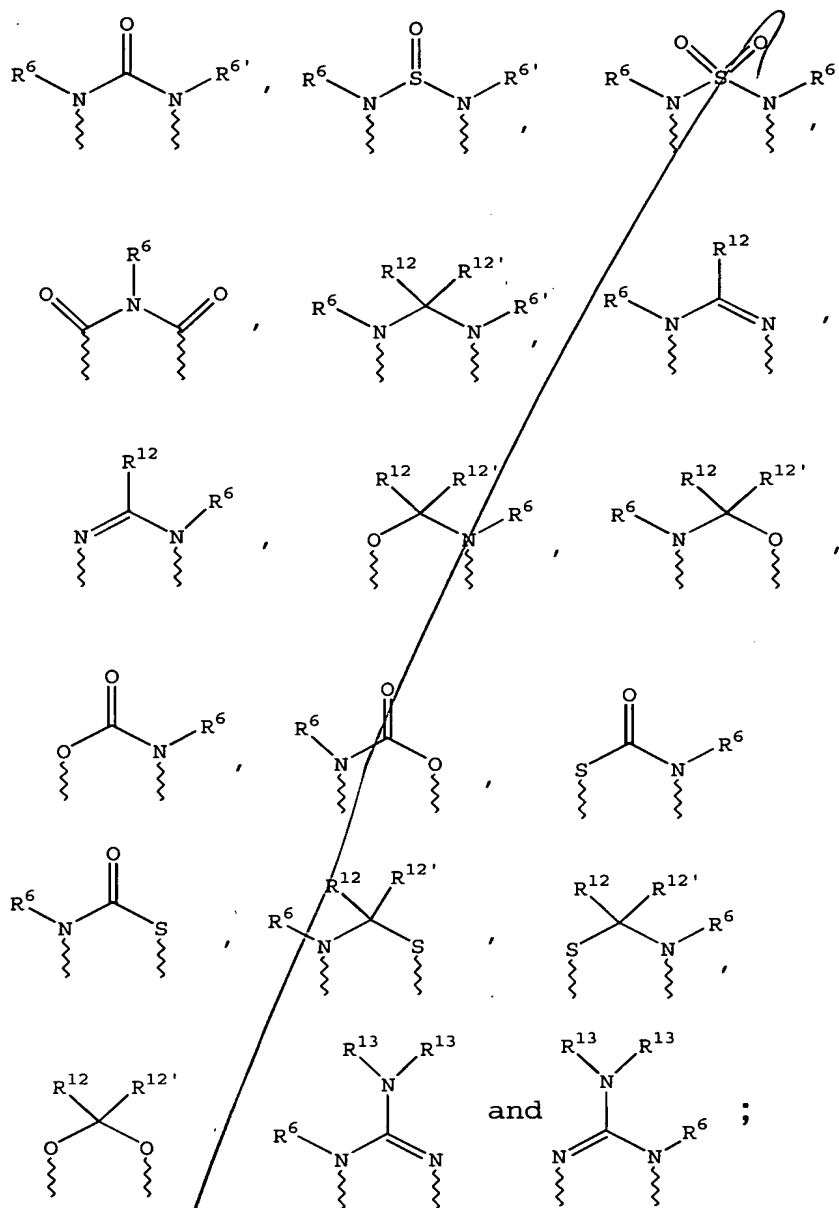
R^{14} is hydrido, a pharmaceutically acceptable cation or $C(W)R^{15}$ where W is O or S and R^{15} is selected from the group consisting of an C_1 - C_6 -alkyl, aryl, C_1 - C_6 -alkoxy, heteroaryl- C_1 - C_6 -alkyl,

15

004450 229760

C₃-C₈-cycloalkyl-C₁-C₆-alkyl, aryloxy, ar-C₁-C₆-alkoxy, ar-C₁-C₆-alkyl, heteroaryl and amino C₁-C₆-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an C₁-C₆-alkyl, aryl, ar-C₁-C₆-alkyl, C₃-C₈-cycloalkyl-C₁-C₆-alkyl, ar-C₁-C₆-alkoxycarbonyl, C₁-C₆-alkoxycarbonyl, and C₁-C₆-alkanoyl radical, or (iii) wherein the amino C₁-C₆-alkyl nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1 or 2;
n is zero, 1 or 2;
p is zero, 1 or 2;
the sum of m + n + p = 1, 2, 3 or 4;
(a) one of X, Y and Z is selected from the group consisting of C(O), NR⁶, O, S, S(O), S(O)₂ and NS(O)₂R⁷, and the remaining two of X, Y and Z are CR⁸R⁹, and CR¹⁰R¹¹, or
(b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of NR⁶C(O), NR⁶S(O), NR⁶S(O)₂, NR⁶S, NR⁶O, SS, NR⁶NR⁶ and OC(O), with the remaining one of X, Y and Z being CR⁸R⁹, or
(c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of



5 wherein wavy lines are bonds to the atoms of the depicted ring;

R^6 and $R^{6'}$ are independently selected from the group consisting of hydrido, formyl, sulfonic- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxycarbonyl- C_1 - C_6 -alkyl, hydroxycarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkylcarbonyl- C_1 - C_6 -alkyl, R^8R^9 -aminocarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -

10

- alkoxycarbonyl-C₁-C₆-alkylcarbonyl, hydroxycarbonyl-C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonyl-C₁-C₆-alkylcarbonyl, C₁-C₆-alkoxycarbonylcarbonyl, hydroxycarbonylcarbonyl, C₁-C₆-alkylcarbonylcarbonyl,
- 5 R⁸R⁹-aminocarbonylcarbonyl, C₁-C₆-alkanoyl, aryl-C₁-C₆-alkyl, aroyl, bis(C₁-C₆-alkoxy-C₁-C₆-alkyl)-C₁-C₆-alkyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-perfluoroalkyl, C₁-C₆-trifluoromethylalkyl, C₁-C₆-perfluoroalkoxy-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-
- 10 alkyl, C₃-C₆-cycloalkyl, heteroarycarbonyl, heterocyclocarbonyl, C₃-C₈-heterocycloalkyl, C₃-C₈-heterocycloalkylcarbonyl, aryl, C₅-C₆-heterocyclo, C₅-C₆-heteroaryl, C₃-C₈-cycloalkyl-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, heteroaryloxy-C₁-C₆-alkyl,
- 15 heteroaryl-C₁-C₆-alkoxy-C₁-C₆-alkyl, heteroarylthio-C₁-C₆-alkyl, arylsulfonyl, C₁-C₆-alkylsulfonyl, C₅-C₆-heteroarylsulfonyl, carboxy-C₁-C₆-alkyl, C₁-C₄-alkoxycarbonyl-C₁-C₆-alkyl, aminocarbonyl, C₁-C₆-alkyl(R⁸N)iminocarbonyl, aryl(R⁸N)iminocarbonyl, C₅-
- 20 C₆-heterocyclo(R⁸N)iminocarbonyl, arylthio-C₁-C₆-alkyl, C₁-C₆-alkylthio-C₁-C₆-alkyl, arylthio-C₃-C₆-alkenyl, C₁-C₄-alkylthio-C₃-C₆-alkenyl, C₅-C₆-heteroaryl-C₁-C₆-alkyl, halo-C₁-C₆-alkanoyl, hydroxy-C₁-C₆-alkanoyl, thiol-C₁-C₆-alkanoyl, C₃-C₆-alkenyl,
- 25 C₃-C₆-alkynyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₅-alkoxycarbonyl, aryloxycarbonyl, NR⁸R⁹-(R⁸)iminomethyl, NR⁸R⁹-C₁-C₅-alkylcarbonyl, hydroxy-

C₁-C₅-alkyl, R⁸R⁹-aminocarbonyl, R⁸R⁹-aminocarbonyl-
C₁-C₆-alkylcarbonyl, hydroxyaminocarbonyl, R⁸R⁹-
aminosulfonyl, R⁸R⁹-aminosulfon-C₁-C₆-alkyl, R⁸R⁹-
amino-C₁-C₆-alkylsulfonyl and an R⁸R⁹-amino-C₁-C₆-
5 alkyl group;

R⁷ is selected from the group consisting of
a arylalkyl, aryl, heteroaryl, heterocyclo, C₁-C₆-
alkyl, C₃-C₆-alkynyl, C₃-C₆-alkenyl, C₁-C₆-
carboxyalkyl and a C₁-C₆-hydroxyalkyl group;

10 R⁸ and R⁹ and R¹⁰ and R¹¹ are independently
selected from the group consisting of a hydrido,
hydroxy, C₁-C₆-alkyl, C₁-C₆-alkanoyl, aroyl, aryl,
ar-C₁-C₆-alkyl, heteroaryl, heteroar-C₁-C₆-alkyl, C₂-
C₆-alkynyl, C₂-C₆-alkenyl, thiol-C₁-C₆-alkyl, C₁-C₆-
15 alkylthio-C₁-C₆-alkyl, cycloalkyl, cycloalkyl-C₁-C₆-
alkyl, heterocycloalkyl-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-
C₆-alkyl, aralkoxy-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-
alkoxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl,
hydroxycarbonyl-C₁-C₆-alkyl, hydroxycarbonylar-C₁-C₆-
20 alkyl, aminocarbonyl-C₁-C₆-alkyl, aryloxy-C₁-C₆-
alkyl, heteroaryloxy-C₁-C₆-alkyl, arylthio-C₁-C₆-
alkyl, heteroarylthio-C₁-C₆-alkyl, the sulfoxide or
sulfone of any said thio substituents, perfluoro-C₁-
C₆-alkyl, trifluoromethyl-C₁-C₆-alkyl, halo-C₁-C₆-
25 alkyl, alkoxycarbonylamino-C₁-C₆-alkyl and an amino-
C₁-C₆-alkyl group wherein the aminoalkyl nitrogen is
(i) unsubstituted or (ii) substituted with one or two

radicals independently selected from the group consisting of C₁-C₆-alkyl, ar-C₁-C₆-alkyl, cycloalkyl and C₁-C₆-alkanoyl, or wherein R⁸ and R⁹ or R¹⁰ and R¹¹ and the carbon to which they are bonded form a carbonyl group, or wherein R⁸ and R⁹ or R¹⁰ and R¹¹, or R⁸ and R¹⁰ together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen, oxygen, or sulfur, with the proviso that only one of R⁸ and R⁹ or R¹⁰ and R¹¹ is hydroxy;

R¹² and R^{12'} are independently selected from the group consisting of a hydrido, C₁-C₆-alkyl, aryl, ar-C₁-C₆-alkyl, heteroaryl, heteroaralkyl, C₂-C₆-alkynyl, C₂-C₆-alkenyl, thiol-C₁-C₆-alkyl, cycloalkyl, cycloalkyl-C₁-C₆-alkyl, heterocycloalkyl-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkoxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl, hydroxycarbonyl-C₁-C₆-alkyl, hydroxycarbonylar-C₁-C₆-alkyl, aminocarbonyl-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, heteroaryloxy-C₁-C₆-alkyl, C₁-C₆-alkylthio-C₁-C₆-alkyl, arylthio-C₁-C₆-alkyl, heteroarylthio-C₁-C₆-alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro-C₁-C₆-alkyl, trifluoromethyl-C₁-C₆-alkyl, halo-C₁-C₆-alkyl, alkoxycarbonylamino-C₁-C₆-alkyl and an amino-C₁-C₆-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii)

substituted with one or two radicals independently selected from the group consisting of C_1-C_6 -alkyl, ar- C_1-C_6 -alkyl, cycloalkyl and C_1-C_6 -alkanoyl;

R^{13} is selected from the group consisting of a hydrido, benzyl, phenyl, C_1-C_6 -alkyl, C_2-C_6 -alkynyl, C_2-C_6 -alkenyl and a C_1-C_6 -hydroxyalkyl group; and

G-A-R-E-Y is a substituent that has a length greater than that of a pentyl group a length that is less than that of an icosyl group, and wherein

G is an aryl or heteroaryl group;

A is selected from the group consisting of

- (1) -O-;
- (2) -S-;
- (3) -NR¹⁷-;
- (4) -CO-N(R¹⁷) or -N(R¹⁷)-CO-, wherein R¹⁷ is hydrogen, C_1-C_4 -alkyl, or phenyl;
- (5) -CO-O- or -O-CO-;
- (6) -O-CO-O-;
- (7) -HC=CH-;
- (8) -NH-CO-NH-;
- (9) -C≡C-;
- (10) -NH-CO-O- or -O-CO-NH-;
- (11) -N=N-;
- (12) -NH-NH-; and
- (13) -CS-N(R¹⁸)- or -N(R¹⁸)-CS-, wherein R¹⁸ is hydrogen C_1-C_4 -alkyl, or phenyl; or

(14) A is absent and G is bonded directly to R;

R is a moiety selected from the group consisting of alkyl, alkoxyalkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroaralkyl, heterocycloalkylalkyl, cycloalkylalkyl, cycloalkoxyalkyl, heterocycloalkoxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, arylthioalkyl, heteroarylthioalkyl, cycloalkylthioalkyl, and a heterocycloalkylthioalkyl group wherein the aryl or heteroaryl or cycloalkyl or heterocycloalkyl substituent is (i) unsubstituted or (ii) substituted with one or two radicals selected from the group consisting of a halo, alkyl, perfluoroalkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, amino, alkoxycarbonylalkyl, alkoxy, C₁-C₂-alkylene-dioxy, hydroxycarbonylalkyl, hydroxycarbonylalkylamino, nitro, hydroxy, hydroxyalkyl, alkanoylamino, and a alkoxycarbonyl group, and R is other than alkyl or alkoxyalkyl when A is -O- or -S-;

E is selected from the group consisting of

- (1) -CO(R¹⁹)- or -(R¹⁹)CO-, wherein R¹⁹ is a heterocycloalkyl, or a cycloalkyl group;
- (2) -CONH- or -HNCO-; and
- (3) -CO-;
- (4) -SO₂-R¹⁹- or -R¹⁹-SO₂-;
- (5) -SO₂-;
- (6) -NH-SO₂- or -SO₂-NH-; or

(7) E is absent and R is bonded directly to Y; and

Y is absent or is selected from the group consisting of a hydrido, alkyl, alkoxy, haloalkyl, aryl, aralkyl, cycloalkyl, heteroaryl, hydroxy, aryloxy, aralkoxy, heteroaryloxy, heteroaralkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, alkenyl, heterocycloalkyl, cycloalkyl, trifluoromethyl, alkoxycarbonyl, and a aminoalkyl group, wherein the aryl or heteroaryl or heterocycloalkyl group is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of an alkanoyl, halo, nitro, aralkyl, aryl, alkoxy, and an amino group wherein the amino nitrogen is (i) unsubstituted or (ii) substituted with one or two groups independently selected from hydrido, alkyl, and an aralkyl group.

53. The compound or salt according to claim 52 wherein said -G-A-R-E-Y substituent contains two to four carbocyclic or heterocyclic rings.

54. The compound or salt according to claim 52 wherein each of the two to four rings is 6-membered.

55. The compound or salt according to claim 52 wherein said -G-A-R-E-Y substituent has a length that is greater than a hexyl group and a length that is less than that of a stearyl group.

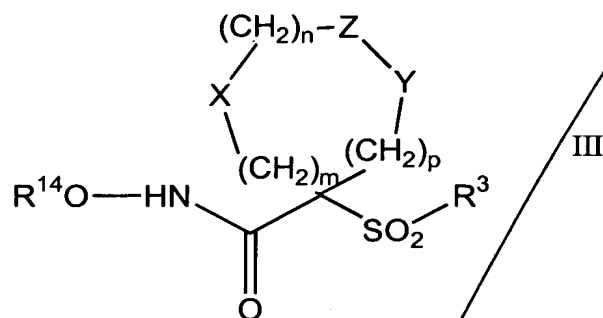
Sub B19

58. The compound or salt according to claim 52 wherein E is absent.

59. The compound or salt according to claim 52 wherein Y is selected from the group consisting of hydrido, an alkyl, alkoxy, perfluoroalkoxy and a perfluoroalkylthio group.

60. The compound or salt according to claim 52 wherein R^{14} is hydrido.

25 62. A compound corresponding in structure
to formula III, below, or a pharmaceutically
acceptable salt thereof



wherein

R^3 is a single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself substituted at its own 4-position when a 6-membered ring and at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of a thiophenoxy, 4-chloro-phenoxy, 3-chlorophenoxy, 4-methoxyphenoxy, 3-benzodioxol-5-yloxy, 3,4-dimethylphenoxy, 4-fluorophenoxy, 4-fluorothiophenoxy, phenoxy, 4-trifluoromethoxyphenoxy, 4-trifluoromethylphenoxy, 4-(trifluoromethylthio)phenoxy, 4-(trifluoromethylthio)thiophenoxy, 4-chloro-3-fluorophenoxy, 4-isopropoxyphenoxy, 4-isopropylphenoxy, (2-methyl-1,3-benzothiazol-5-yl)oxy, 4-(1H-imidazol-1-yl)phenoxy, 4-chloro-3-methylphenoxy, 3-methyl-phenoxy, 4-ethoxyphenoxy, 3,4-difluorophenoxy, 4-chloro-3-methylphenoxy, 4-fluoro-3-chlorophenoxy, 4-(1H-1,2,4-triazol-1-yl)phenoxy, 3,5-difluorophenoxy, 3,4-dichlorophenoxy, 4-cyclopentylphenoxy, 4-bromo-3-methylphenoxy, 4-bromophenoxy, 4-methylthiophenoxy, 4-phenylphenoxy, 4-benzylphenoxy, 6-quinolinyloxy, 4-amino-3-methylphenoxy, 3-methoxyphenoxy, 5,6,7,8-tetrahydro-2-naphthalenyloxy, 3-hydroxymethylphenoxy, and a 4-benzyloxyphenoxy group;

60430-227760

R^{14} is hydrido, a pharmaceutically acceptable cation or $C(W)R^{15}$ where W is O or S and R^{15} is selected from the group consisting of a C_1-C_6 -alkyl, aryl, C_1-C_6 -alkoxy, heteroaryl- C_1-C_6 -alkyl, C_3-C_8 -cycloalkyl- C_1-C_6 -alkyl, aryloxy, ar- C_1-C_6 -alkoxy, ar- C_1-C_6 -alkyl, heteroaryl and amino C_1-C_6 -alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an C_1-C_6 -alkyl, aryl, ar- C_1-C_6 -alkyl, C_3-C_8 -cycloalkyl- C_1-C_6 -alkyl, ar- C_1-C_6 -alkoxycarbonyl, C_1-C_6 -alkoxycarbonyl, and C_1-C_6 -alkanoyl radical, or (iii) wherein the amino C_1-C_6 -alkyl nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1 or 2;

n is zero, 1 or 2;

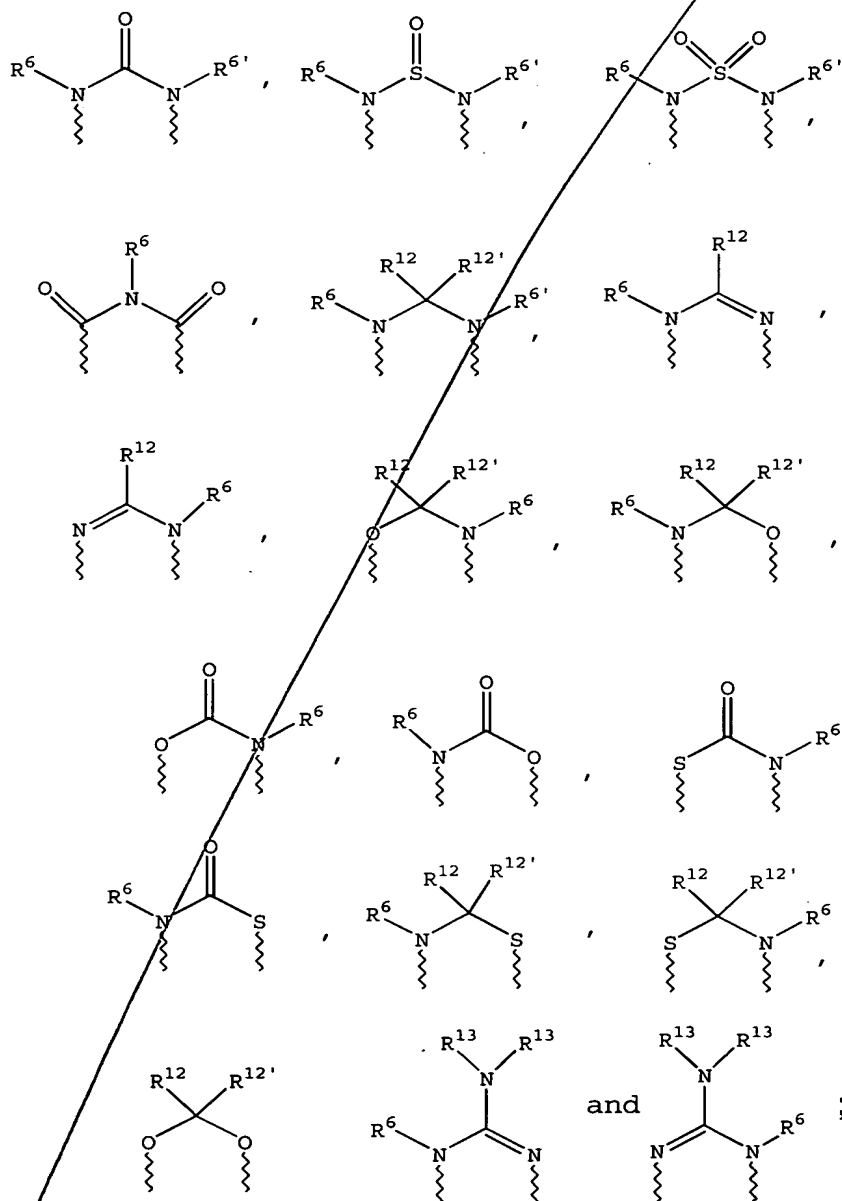
p is zero, 1 or 2;

the sum of $m + n + p = 1, 2, 3$ or 4;

(a) one of X, Y and Z is selected from the group consisting of $C(O)$, NR^6 , O, S, $S(O)$, $S(O)_2$ and $NS(O)_2R^7$, and the remaining two of X, Y and Z are CR^8R^9 , and $CR^{10}R^{11}$, or

(b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of $NR^6C(O)$, $NR^6S(O)$, $NR^6S(O)_2$, NR^6S , NR^6O , SS , NR^6NR^6 and $OC(O)$, with the remaining one of X, Y and Z being CR^8R^9 , or

(c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of



wherein wavy lines are bonds to the atoms
10 of the depicted ring;

R^6 and $R^{6'}$ are independently selected from the group consisting of hydrido, formyl, sulfonic- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxycarbonyl- C_1 - C_6 -alkyl, hydroxycarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkylcarbonyl- C_1 - C_6 -alkyl, R^8R^9 -aminocarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxycarbonyl- C_1 - C_6 -alkylcarbonyl, hydroxycarbonyl- C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -alkylcarbonyl- C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -alkoxycarbonylcarbonyl, hydroxycarbonylcarbonyl, C_1 - C_6 -alkylcarbonylcarbonyl, R^8R^9 -aminocarbonylcarbonyl, C_1 - C_6 -alkanoyl, aryl- C_1 - C_6 -alkyl, aroyl, bis(C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl)- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_1 - C_6 -perfluoroalkyl, C_1 - C_6 -trifluoromethylalkyl, C_1 - C_6 -perfluoroalkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, heteroarycarbonyl, heterocyclocarbonyl, C_3 - C_8 -heterocycloalkyl, C_3 - C_8 -heterocycloalkylcarbonyl, aryl, C_5 - C_6 -heterocyclo, C_5 - C_6 -heteroaryl, C_3 - C_8 -cycloalkyl- C_1 - C_6 -alkyl, aryloxy- C_1 - C_6 -alkyl, heteroaryloxy- C_1 - C_6 -alkyl, heteroaryl- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, heteroarylthio- C_1 - C_6 -alkyl, arylsulfonyl, C_1 - C_6 -alkylsulfonyl, C_5 - C_6 -heteroarylsulfonyl, carboxy- C_1 - C_6 -alkyl, C_1 - C_4 -alkoxycarbonyl- C_1 - C_6 -alkyl, aminocarbonyl, C_1 - C_6 -alkyl(R^8N)iminocarbonyl, aryl(R^8N)iminocarbonyl, C_5 - C_6 -heterocyclo(R^8N)iminocarbonyl, arylthio- C_1 - C_6 -alkyl, C_1 - C_6 -alkylthio- C_1 - C_6 -alkyl, arylthio- C_3 - C_6 -alkenyl, C_1 - C_4 -alkylthio- C_3 - C_6 -alkenyl, C_5 - C_6 -

heteroaryl-C₁-C₆-alkyl, halo-C₁-C₆-alkanoyl, hydroxy-C₁-C₆-alkanoyl, thiol-C₁-C₆-alkanoyl, C₃-C₆-alkenyl, C₃-C₆-alkynyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₅-alkoxycarbonyl, aryloxycarbonyl, NR⁸R⁹-

- 5 (R⁸)iminomethyl, NR⁸R⁹-C₁-C₅-alkylcarbonyl, hydroxy-C₁-C₅-alkyl, R⁸R⁹-aminocarbonyl, R⁸R⁹-aminocarbonyl-C₁-C₆-alkylcarbonyl, hydroxyaminocarbonyl, R⁸R⁹-aminosulfonyl, R⁸R⁹-aminosulfon-C₁-C₆-alkyl, R⁸R⁹-amino-C₁-C₆-alkylsulfonyl and an R⁸R⁹-amino-C₁-C₆-alkyl group;
- 10

R⁷ is selected from the group consisting of a arylalkyl, aryl, heteroaryl, heterocyclo, C₁-C₆-alkyl, C₃-C₆-alkynyl, C₃-C₆-alkenyl, C₁-C₆-carboxyalkyl and a C₁-C₆-hydroxyalkyl group;

- 15 R⁸ and R⁹ and R¹⁰ and R¹¹ are independently selected from the group consisting of a hydrido, hydroxy, C₁-C₆-alkyl, C₁-C₆-alkanoyl, aroyl, aryl, ar-C₁-C₆-alkyl, heteroaryl, heteroar-C₁-C₆-alkyl, C₂-C₆-alkynyl, C₂-C₆-alkenyl, thiol-C₁-C₆-alkyl, C₁-C₆-alkylthio-C₁-C₆-alkyl, cycloalkyl, cycloalkyl-C₁-C₆-alkyl, heterocycloalkyl-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, aralkoxy-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkoxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl, hydroxycarbonyl-C₁-C₆-alkyl, hydroxycarbonylar-C₁-C₆-alkyl, aminocarbonyl-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, heteroaryloxy-C₁-C₆-alkyl, arylthio-C₁-C₆-alkyl, heteroarylthio-C₁-C₆-alkyl, the sulfoxide or
- 20
- 25

667430 463760

sulfone of any said thio substituents, perfluoro-C₁-C₆-alkyl, trifluoromethyl-C₁-C₆-alkyl, halo-C₁-C₆-alkyl, alkoxycarbonylamino-C₁-C₆-alkyl and an amino-C₁-C₆-alkyl group wherein the aminoalkyl nitrogen is

5 (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C₁-C₆-alkyl, ar-C₁-C₆-alkyl, cycloalkyl and C₁-C₆-alkanoyl, or wherein R⁸ and R⁹ or R¹⁰ and R¹¹ and the carbon to which they are bonded form a

10 carbonyl group, or wherein R⁸ and R⁹ or R¹⁰ and R¹¹, or R⁸ and R¹⁰ together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen,

15 oxygen, or sulfur, with the proviso that only one of R⁸ and R⁹ or R¹⁰ and R¹¹ is hydroxy;

R¹² and R^{12'} are independently selected from the group consisting of a hydrido, C₁-C₆-alkyl, aryl, ar-C₁-C₆-alkyl, heteroaryl, heteroaralkyl, C₂-C₆-alkynyl, C₂-C₆-alkenyl, thiol-C₁-C₆-alkyl,

20 cycloalkyl, cycloalkyl-C₁-C₆-alkyl, heterocycloalkyl-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkoxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl, hydroxycarbonyl-C₁-C₆-alkyl, hydroxycarbonylar-C₁-C₆-alkyl,

25 aminocarbonyl-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, heteroaryloxy-C₁-C₆-alkyl, C₁-C₆-alkylthio-C₁-C₆-alkyl, arylthio-C₁-C₆-alkyl, heteroarylthio-C₁-C₆-

alkyl, the sulfoxide or sulfone of any said thio
substituents, perfluoro-C₁-C₆-alkyl, trifluoromethyl-
C₁-C₆-alkyl, halo-C₁-C₆-alkyl, alkoxycarbonylamino-
C₁-C₆-alkyl and an amino-C₁-C₆-alkyl group wherein
5 the aminoalkyl nitrogen is (i) unsubstituted or (ii)
substituted with one or two radicals independently
selected from the group consisting of C₁-C₆-alkyl,
ar-C₁-C₆-alkyl, cycloalkyl and C₁-C₆-alkanoyl; and

R¹³ is selected from the group consisting
10 of a hydrido, benzyl, phenyl, C₁-C₆-alkyl, C₂-C₆-
alkynyl, C₂-C₆-alkenyl and a C₁-C₆-hydroxyalkyl
group.

63. The compound or salt according to
15 claim 62 wherein the sum of m + n + p = 1 or 2.

64. The compound or salt according to
claim 62 wherein Z is O, S or NR⁶.

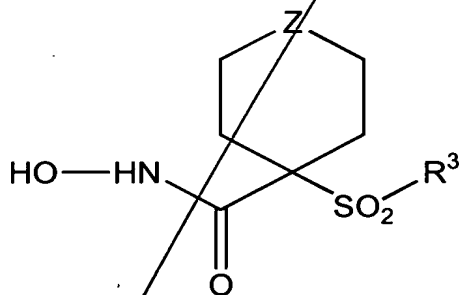
20 65. The compound or salt according to
claim 62 wherein R⁶ is selected from the group
consisting of C₃-C₆-cycloalkyl, C₁-C₆-alkyl, C₃-C₆-
alkenyl, C₃-C₆-alkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl,
amino-C₁-C₆-alkyl, aminosulfonyl, heteroaryl-C₁-C₆-
25 ~~alkyl, aryloxycarbonyl, and C₁-C₆-alkoxycarbonyl.~~

66. The compound or salt according to
claim 62 wherein m = n = ~~zero~~, p = 1, and Y is NR⁶.

Sub B14 67. ~~The compound or salt according to~~
~~claim 62 wherein R¹⁴ is hydrido.~~

68. The compound or salt according to claim 62 wherein W of the $C(W)R^{15}$ is O and R^{15} is a C_1 - C_6 -alkyl, aryl, C_1 - C_6 -alkoxy, heteroaryl- C_1 - C_6 -alkyl, C_3 - C_8 -cycloalkyl- C_1 - C_6 -alkyl, or aryloxy group.

69. A compound corresponding in structure to formula IV, below, or a pharmaceutically acceptable salt thereof



IV

wherein R^3 is a single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself substituted at its own 4-position when a 6-membered ring or at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of one other single-ringed aryl or heteroaryl group, a C_3 - C_{14} alkyl group, a N-piperidyl group, a N-piperazinyl group, a phenoxy group, a thiophenoxy group, a 4-thiopyridyl group, a phenylazo group and a benzamido group; and

Z is selected group the group consisting of O, S, NR^6 , SO, SO_2 , and NSO_2R^7 ,

wherein R^6 is selected from the group consisting of hydrido, C_1 - C_5 -alkyl, C_1 - C_5 -alkanoyl, benzyl, benzoyl, C_3 - C_5 -alkynyl, C_3 - C_5 -alkenyl, C_1 - C_3 -alkoxy- C_1 - C_4 -alkyl, C_3 - C_6 -cycloalkyl, heteroaryl- C_1 -
5 C_6 -alkyl, C_1 - C_5 -hydroxyalkyl, C_1 - C_5 -carboxyalkyl, C_1 - C_5 -alkoxy C_1 - C_5 -alkylcarbonyl, and NR^8R^9 - C_1 - C_5 -alkylcarbonyl or NR^8R^9 - C_1 - C_5 -alkyl wherein R^8 and R^9 are independently hydrido, C_1 - C_5 -alkyl, C_1 - C_5 -alkoxycarbonyl or aryl- C_1 - C_5 -alkoxycarbonyl, or NR^8R^9
10 together form a heterocyclic ring containing 5- to 8-atoms in the ring; and

R^7 is selected from the group consisting of a arylalkyl, aryl, heteroaryl, heterocyclo, C_1 - C_6 -alkyl, C_3 - C_6 -alkynyl, C_3 - C_6 -alkenyl, C_1 - C_6 -
15 carboxyalkyl and a C_1 - C_6 -hydroxyalkyl group.

70. The compound or salt according to claim 69 wherein R^3 has a length that is greater than that of a pentyl group and a length that is less than
20 that of an icosyl group.

71. The compound or salt according to claim 69 wherein Z is O, S or NR^6 .

25 72. The compound or salt according to claim 69 wherein R^6 is selected from the group consisting of C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkynyl,

amino-C₁-C₆-alkyl, aminosulfonyl, heteroaryl-C₁-C₆-alkyl, aryloxy carbonyl, and C₁-C₆-alkoxy carbonyl.

73. The compound or salt according to
5 claim 69 wherein said R³ radical is the substituent
G-A-R-E-Y, wherein

G is an aryl or heteroaryl group;

A is selected from the group

consisting of

- 10 (1) -O-;
- (2) -S-;
- (3) -NR¹⁷-;
- (4) -CO-N(R¹⁷) or -N(R¹⁷)-CO-, wherein R¹⁷
is hydrogen, C₁-C₄-alkyl, or phenyl;
- 15 (5) -CO-O- or -O-CO-;
- (6) -O-CO-O-;
- (7) -HC=CH-;
- (8) -NH-CO-NH-;
- (9) -C≡C-;
- 20 (10) -NH-CO-O- or -O-CO-NH-;
- (11) -N=N-;
- (12) -NH-NH-; and
- (13) -CS-N(R¹⁸)- or -N(R¹⁸)-CS-, wherein
R¹⁸ is hydrogen C₁-C₄-alkyl, or
- 25 phenyl; or
- (14) A is absent and G is bonded directly
to R;
- R is a moiety selected from the group
consisting of alkyl, alkoxyalkyl, aryl, heteroaryl,

064433-04430
cycloalkyl, heterocycloalkyl, aralkyl, heteroaralkyl,
heterocycloalkylalkyl, cycloalkylalkyl,
cycloalkoxyalkyl, heterocycloalkoxyalkyl,
aryloxyalkyl, heteroaryloxyalkyl, arylthioalkyl,
5 heteroarylthioalkyl, cycloalkylthioalkyl, and a
heterocycloalkylthioalkyl group wherein the aryl or
heteroaryl or cycloalkyl or heterocycloalkyl
substituent is (i) unsubstituted or (ii) substituted
with one or two radicals selected from the group
10 consisting of a halo, alkyl, perfluoroalkyl,
perfluoroalkoxy, perfluoroalkylthio,
trifluoromethylalkyl, amino, alkoxycarbonylalkyl,
alkoxy, C₁-C₂-alkylene-dioxy, hydroxycarbonylalkyl,
hydroxycarbonylalkylamino, nitro, hydroxy,
15 hydroxyalkyl, alkanoylamino, and a alkoxycarbonyl
group, and R is other than alkyl or alkoxyalkyl when
A is -O- or -S-;

E is selected from the group consisting of

- (1) -CO(R¹⁹)- or -(R¹⁹)CO-, wherein R¹⁹ is
20 a heterocycloalkyl, or a cycloalkyl
group;
(2) -CONH- or -HNCO-; and
(3) -CO-;
(4) -SO₂-R¹⁹- or -R¹⁹-SO₂-;
25 (5) -SO₂-;
(6) -NH-SO₂- or -SO₂-NH-; or
(7) E is absent and R is bonded directly
to Y; and

Y is absent or is selected from the group
30 consisting of a hydrido, alkyl, alkoxy, haloalkyl,

aryl, aralkyl, cycloalkyl, heteroaryl, hydroxy,
aryloxy, aralkoxy, heteroaryloxy, heteroaralkyl,
perfluoroalkoxy, perfluoroalkylthio,
trifluoromethylalkyl, alkenyl, heterocycloalkyl,
5 cycloalkyl, trifluoromethyl, alkoxycarbonyl, and a
aminoalkyl group, wherein the aryl or heteroaryl or
heterocycloalkyl group is (i) unsubstituted or (ii)
substituted with one or two radicals independently
selected from the group consisting of an alkanoyl,
10 halo, nitro, aralkyl, aryl, alkoxy, and an amino
group wherein the amino nitrogen is (i) unsubstituted
or (ii) substituted with one or two groups
independently selected from hydrido, alkyl, and an
aralkyl group.

15

74. The compound or salt according to
claim 69 wherein said -G-A-R-E-Y substituent contains
two to four carbocyclic or heterocyclic rings.

20

75. The compound or salt according to
claim 69 wherein each of the two to four rings is 6-
membered.

25

76. The compound or salt according to
claim 69 wherein said -G-A-R-E-Y substituent has a
length that is greater than a hexyl group and a
length that is less than that of a stearyl group.

30

77. The compound or salt according to
claim 69 wherein A is -O- or -S-.

5 79. The compound or salt according to
claim 69 wherein E is absent.

81. The compound or salt according to claim 69 wherein R³ is a radical that is comprised of a single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself substituted at its own 4-position when a 6-membered ring and at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of a thiophenoxy, 4-chlorophenoxy, 3-chlorophenoxy, 4-methoxyphenoxy, 3-benzodioxol-5-yloxy, 3,4-dimethylphenoxy, 4-fluorophenoxy, 4-fluorothiophenoxy, phenoxy, 4-trifluoromethoxyphenoxy, 4-trifluoromethylphenoxy, 4-(trifluoromethylthio)phenoxy, 4-(trifluoromethylthio)thiophenoxy, 4-chloro-3-fluorophenoxy, 4-isopropoxyphenoxy, 4-isopropylphenoxy, (2-methyl-1,3-benzothiazol-5-yl)oxy, 4-(1H-imidazol-1-yl)phenoxy, 4-chloro-3-methylphenoxy, 3-methylphenoxy, 4-ethoxyphenoxy, 3,4-difluorophenoxy, 4-chloro-3-methylphenoxy, 4-fluoro-3-chlorophenoxy, 4-(1H-1,2,4-triazol-1-yl)phenoxy,

3,5-difluorophenoxy, 3,4-dichlorophenoxy, 4-cyclopentylphenoxy, 4-bromo-3-methylphenoxy, 4-bromophenoxy, 4-methylthiophenoxy, 4-phenylphenoxy, 4-benzylphenoxy, 6-quinolinyloxy, 4-amino-3-methylphenoxy, 3-methoxyphenoxy, 5,6,7,8-tetrahydro-2-naphthalenyloxy, 3-hydroxymethylphenoxy, N-piperidyl, N-piperazinyl and a 4-benzyloxyphenoxy group.

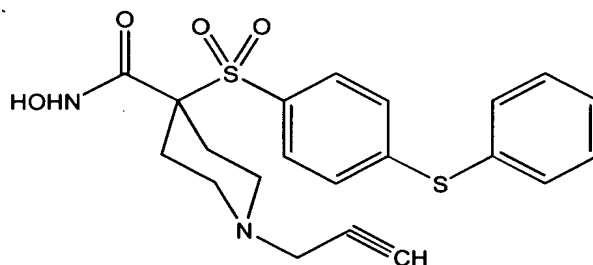
Sub B15/10
~~82. The compound or salt according to claim 69 wherein said R³ group is a PhR²³ group, wherein Ph is a phenyl ring that is substituted at its 4-position by an R²³ group that is a substituent selected from the group consisting of another single-
15 ringed aryl or heteroaryl group, a piperidyl group, a piperazinyl group, a phenoxy group, a thiophenoxy group, a phenylazo group and a benzamido group.~~

~~83. The compound or salt according to
20 claim 82 wherein said R²³ group is itself substituted with a moiety that is selected from the group consisting of a halogen, a C₁-C₄ alkoxy group, a C₁-C₄ alkyl group, a dimethylamino group, a carboxyl C₁-C₃ alkylene group, a C₁-C₄ alkoxy carbonyl C₁-C₃
25 alkylene group, a trifluoromethylthio group, a trifluoromethoxy group, a trifluoromethyl group and a carboxamido C₁-C₃ alkylene group, or is substituted at the meta- and para-positions by a methylenedioxy group.~~

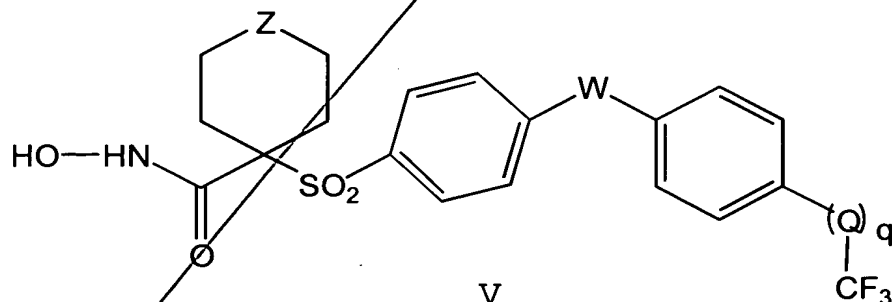
84. The compound or salt according to claim 83 wherein said R^{23} group is substituted at the para-position.

5 85. The compound or salt according to claim 84 wherein said R^{23} group is phenoxy.

86. The compound or salt according to claim 69 wherein said inhibitor corresponds in
10 structure to the formula



66-39-223466
Sal B16
87. A compound corresponding in structure to formula V, below, or a pharmaceutically acceptable
15 salt thereof



20 wherein
Z is O, S or NR^6 ;

W and Q are independently oxygen (O), NR⁶
or sulfur (S),

R⁶ is selected from the group consisting of
C₃-C₆-cycloalkyl, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-
5 alkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl,
aminosulfonyl, heteroaryl-C₁-C₆-alkyl,
aryloxycarbonyl, and C₁-C₆-alkoxycarbonyl; and

q is zero or one such that when q is zero,
Q is absent and the trifluoromethyl group is bonded
10 directly to the depicted phenyl ring.

88. The compound or salt according to
claim 87 wherein q is zero.

15 89. The compound or salt according to
claim 87 wherein W is O.

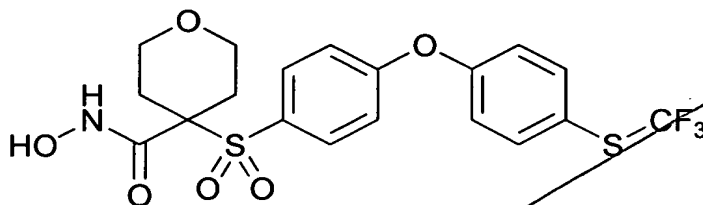
90. The compound or salt according to
claim 89 wherein q is zero.

20 91. The compound or salt according to
claim 89 wherein q is one and Q is O.

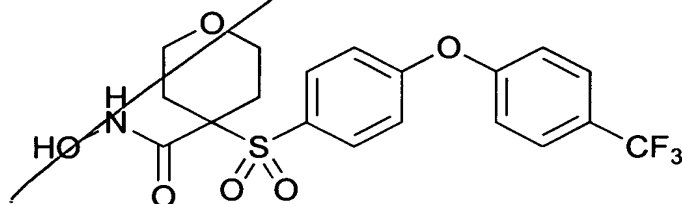
92. The compound or salt according to
25 claim 89 wherein q is one and Q is S.

93. The compound or salt according to
claim 87 wherein said inhibitor corresponds in
structure to the formula

504T20 234T20

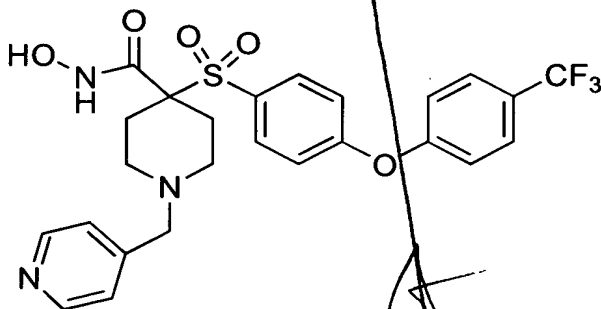


94. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula



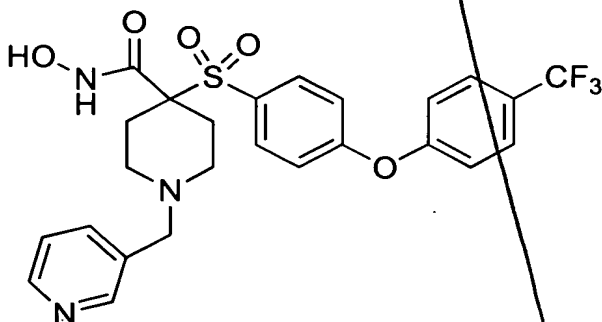
5

95. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula

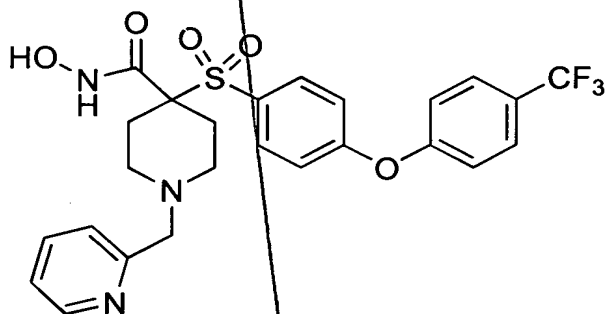


10

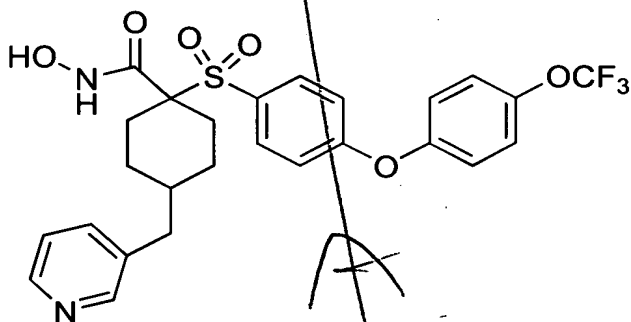
96. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula



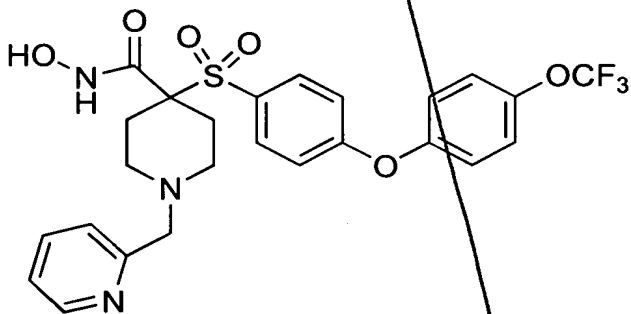
97. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula



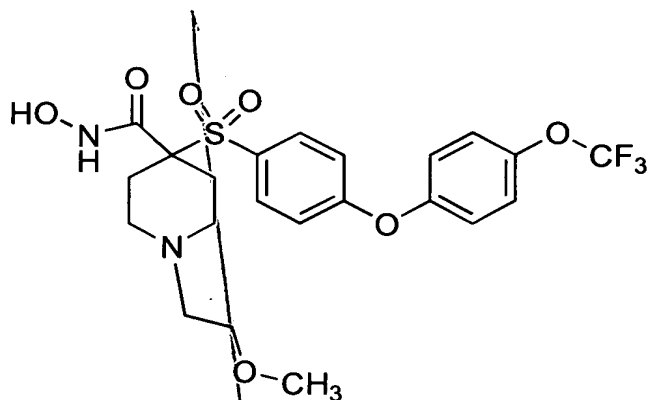
5 98. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula



10 99. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula

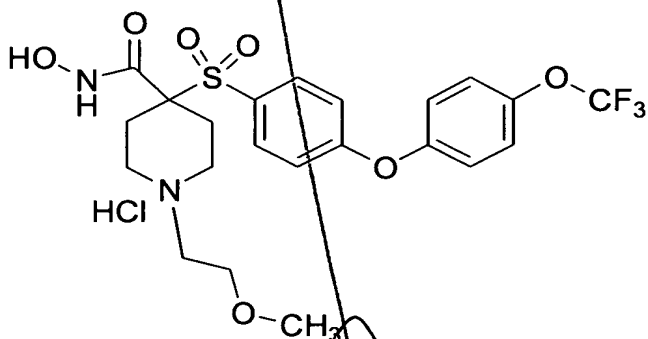


15 100. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula



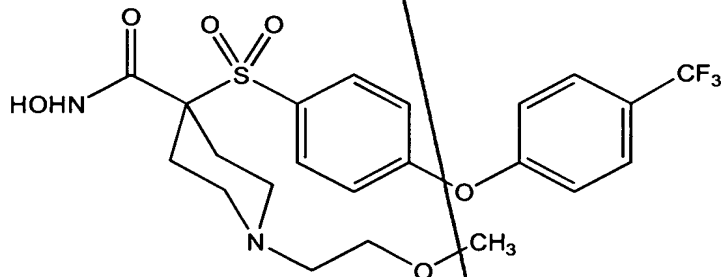
101. The compound or salt according to claim 100 wherein said inhibitor corresponds in structure to the formula

5

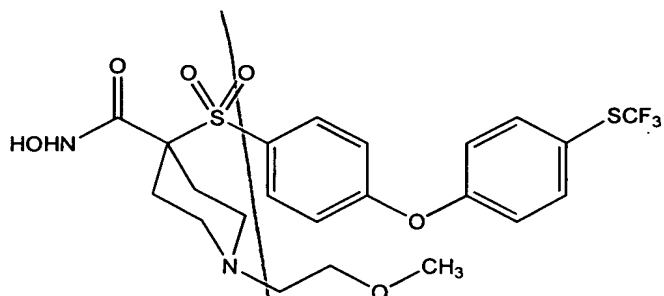


102. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula

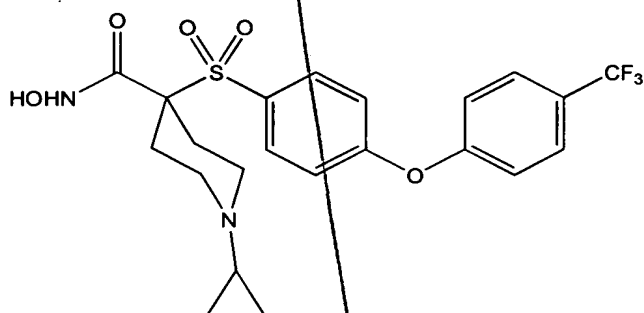
10



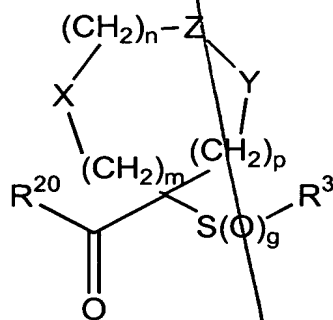
103. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula



104. The compound or salt according to claim 87 wherein said inhibitor corresponds in structure to the formula



105. A compound corresponding in structure to formula VI, below



VI

wherein

g is zero, 1 or 2;

R^3 is an optionally substituted aryl or optionally substituted heteroaryl radical, and when

DEFT 50 223760

said aryl or heteroaryl radical is substituted, the substituent is (a) selected from the group consisting of an optionally substituted cycloalkyl, heterocycloalkyl, aryl, heteroaryl, aralkyl, heteroaralkyl, aralkoxy, heteroaralkoxy, aralkoxyalkyl, aryloxyalkyl, aralkanoylalkyl, arylcarbonylalkyl, aralkylaryl, aryloxyalkylaryl, aralkoxyaryl, arylazoaryl, arylhydrazinoaryl, alkylthioaryl, arylthioalkyl, alkylthioaralkyl, aralkylthioalkyl, an aralkylthioaryl radical, the sulfoxide or sulfone of any of the thio substituents, and a fused ring structure comprising two or more 5- or 6-membered rings selected from the group consisting of aryl, heteroaryl, cycloalkyl and heterocycloalkyl, and (b) is itself optionally substituted with one or more substituents independently selected from the group consisting of a cyano, perfluoroalkyl, trifluoromethoxy, trifluoromethylthio, haloalkyl, trifluoromethylalkyl, aralkoxycarbonyl, aryloxycarbonyl, hydroxy, halo, alkyl, alkoxy, nitro, thiol, hydroxycarbonyl, aryloxy, arylthio, aralkyl, aryl, arylcarbonylamino, heteroaryloxy, heteroarylthio, heteroaralkyl, cycloalkyl, heterocyclooxy, heterocyclothio, heterocycloamino, cycloalkyloxy, cycloalkylthio, heteroaralkoxy, heteroaralkylthio, aralkoxy, aralkylthio, aralkylamino, heterocyclo, heteroaryl, arylazo, hydroxycarbonylalkoxy, alkoxycarbonylalkoxy, alkanoyl, arylcarbonyl, aralkanoyl, alkanoyloxy, aralkanoyloxy, hydroxyalkyl, hydroxyalkoxy, alkylthio, alkoxyalkylthio, alkoxycarbonyl, aryloxyalkoxyaryl, arylthioalkylthioaryl, aryloxyalkylthioaryl, arylthioalkoxyaryl,

hydroxycarbonylalkoxy, hydroxycarbonylalkylthio,
alkoxycarbonylalkoxy, alkoxycarbonylalkylthio, amino,

5 wherein the amino nitrogen is (i) unsubstituted,
 or (ii) substituted with one or two substituents
 that are independently selected from the group
 consisting of an alkyl, aryl, heteroaryl,
 aralkyl, cycloalkyl, aralkoxycarbonyl,
 alkoxycarbonyl, arylcarbonyl, aralkanoyl,
 heteroarylcarbonyl, heteroaralkanoyl and an
10 alkanoyl group, or (iii) wherein the amino
 nitrogen and two substituents attached thereto
 form a 5- to 8-membered heterocyclo or
 heteroaryl ring containing zero to two
 additional heteroatoms that are nitrogen, oxygen
15 or sulfur and which ring itself is (a)
 unsubstituted or (b) substituted with one or two
 groups independently selected from the group
 consisting of an aryl, alkyl, heteroaryl,
 aralkyl, heteroaralkyl, hydroxy, alkoxy,
20 alkanoyl, cycloalkyl, heterocycloalkyl,
 alkoxycarbonyl, hydroxyalkyl, trifluoromethyl,
 benzofused heterocycloalkyl, hydroxyalkoxyalkyl,
 aralkoxycarbonyl, hydroxycarbonyl,
 aryloxycarbonyl, benzofused heterocycloalkoxy,
25 benzofused cycloalkylcarbonyl, heterocyclo-
 alkylcarbonyl, and a cycloalkylcarbonyl group,
 carbonylamino

 wherein the carbonylamino nitrogen is (i)
 unsubstituted, or (ii) is the reacted amine of
30 an amino acid, or (iii) substituted with one or
 two radicals selected from the group consisting
 of an alkyl, hydroxyalkyl, hydroxyheteroaralkyl,
 cycloalkyl, aralkyl, trifluoromethylalkyl,

heterocycloalkyl, benzofused heterocycloalkyl,
benzofused heterocycloalkyl, benzofused
cycloalkyl, and an N,N-dialkylsubstituted
alkylamino-alkyl group, or (iv) the carboxamido
5 nitrogen and two substituents bonded thereto
together form a 5- to 8-membered heterocyclo,
heteroaryl or benzofused heterocycloalkyl ring
that is itself unsubstituted or substituted with
one or two radicals independently selected from
10 the group consisting of an alkyl,
alkoxycarbonyl, nitro, heterocycloalkyl,
hydroxy, hydroxycarbonyl, aryl, aralkyl,
heteroaralkyl and an amino group,
wherein the amino nitrogen is
15 (i) unsubstituted, or (ii) substituted with
one or two substituents that are
independently selected from the group
consisting of alkyl, aryl, and heteroaryl,
or (iii) wherein the amino nitrogen and two
20 substituents attached thereto form a 5- to
8-membered heterocyclo or heteroaryl ring,
and an aminoalkyl group
wherein the aminoalkyl nitrogen is (i)
unsubstituted, or (ii) substituted with one or two
25 substituents independently selected from the group
consisting of an alkyl, aryl, aralkyl, cycloalkyl,
aralkoxycarbonyl, alkoxycarbonyl, and an alkanoyl
group, or (iii) wherein the aminoalkyl nitrogen and
two substituents attached thereto form a 5- to 8-
30 membered heterocyclo or heteroaryl ring, or is
an aryl or heteroaryl group that is substituted with
a nucleophilically displaceable leaving group;

m is zero, 1 or 2;

n is zero, 1 or 2;

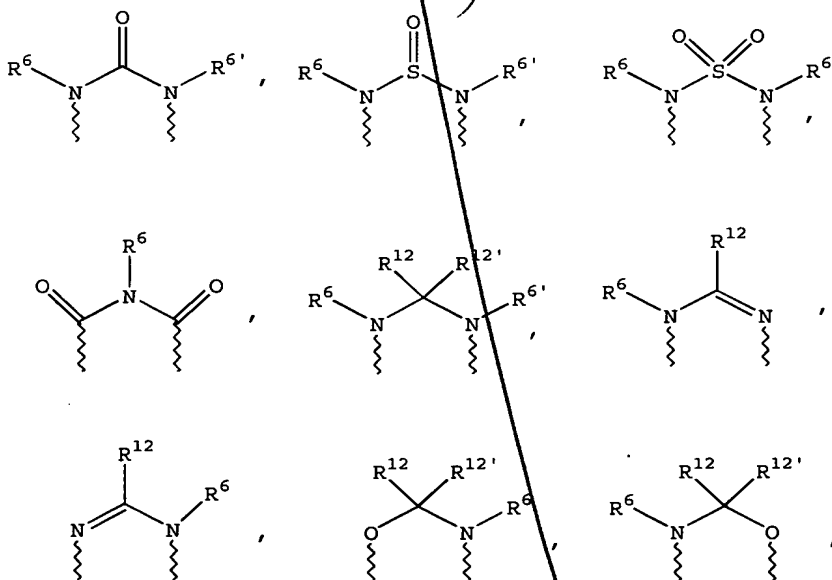
p is zero, 1 or 2;

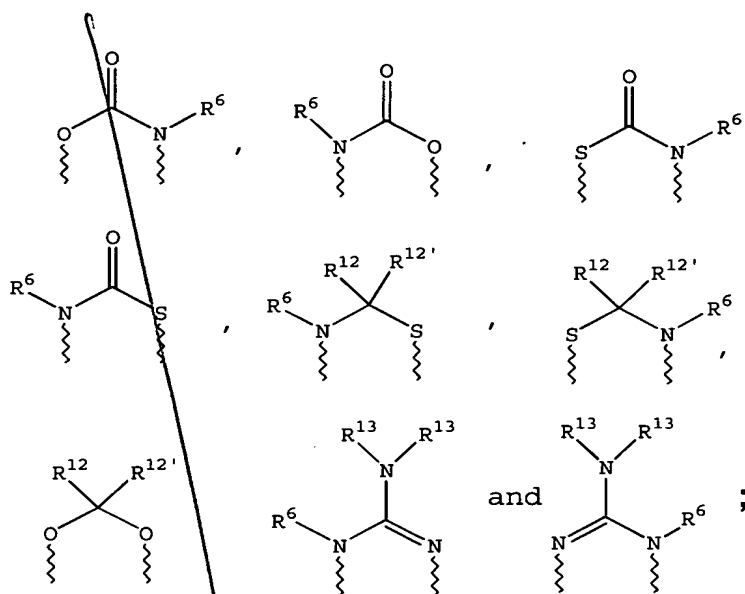
the sum of $m + n + p = 1, 2, 3$ or 4;

5 (a) one of X, Y and Z is selected from the group consisting of $C(O)$, NR^6 , O, S, $S(O)$, $S(O)_2$ and $NS(O)_2R^7$, and the remaining two of X, Y and Z are CR^8R^9 , and $CR^{10}R^{11}$, or

10 (b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of $NR^6C(O)$, $NR^6S(O)$, $NR^6S(O)_2$, NR^6S , NR^6O , SS, NR^6NR^6 and $OC(O)$, with the remaining one of X, Y and Z being CR^8R^9 , or

15 (c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of





wherein wavy lines are bonds to the atoms of the depicted ring;

- 5 R^6 and R^6' are independently selected from the group consisting of hydrido, formyl, sulfonic- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxycarbonyl- C_1 - C_6 -alkyl, hydroxycarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkylcarbonyl- C_1 - C_6 -alkyl, R^8R^9 -aminocarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxycarbonyl- C_1 - C_6 -alkylcarbonyl, hydroxycarbonyl- C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -alkylcarbonyl- C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -alkoxycarbonylcarbonyl, hydroxycarbonylcarbonyl, C_1 - C_6 -alkylcarbonylcarbonyl, R^8R^9 -aminocarbonylcarbonyl, C_1 - C_6 -alkanoyl, aryl- C_1 - C_6 -alkyl, aroyl, bis(C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl)- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_1 - C_6 -perfluoroalkyl, C_1 - C_6 -trifluoromethylalkyl, C_1 - C_6 -perfluoroalkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, heteroarycarbonyl,
- 10
- 15

heterocyclocarbonyl, C₃-C₈-heterocycloalkyl, C₃-C₈-
heterocycloalkylcarbonyl, aryl, C₅-C₆-heterocyclo,
C₅-C₆-heteroaryl, C₃-C₈-cycloalkyl-C₁-C₆-alkyl,
aryloxy-C₁-C₆-alkyl, heteroaryloxy-C₁-C₆-alkyl,
5 heteroaryl-C₁-C₆-alkoxy-C₁-C₆-alkyl, heteroarylthio-
C₁-C₆-alkyl, arylsulfonyl, C₁-C₆-alkylsulfonyl, C₅-
C₆-heteroarylsulfonyl, carboxy-C₁-C₆-alkyl, C₁-C₄-
alkoxycarbonyl-C₁-C₆-alkyl, aminocarbonyl, C₁-C₆-
alkyl(R⁸N)iminocarbonyl, aryl(R⁸N)iminocarbonyl, C₅-
10 C₆-heterocyclo(R⁸N)iminocarbonyl, arylthio-C₁-C₆-
alkyl, C₁-C₆-alkylthio-C₁-C₆-alkyl, arylthio-C₃-C₆-
alkenyl, C₁-C₄-alkylthio-C₃-C₆-alkenyl, C₅-C₆-
heteroaryl-C₁-C₆-alkyl, halo-C₁-C₆-alkanoyl, hydroxy-
C₁-C₆-alkanoyl, thiol-C₁-C₆-alkanoyl, C₃-C₆-alkenyl,
15 C₃-C₆-alkynyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₅-
alkoxycarbonyl, aryloxycarbonyl, NR⁸R⁹-
(R⁸)iminomethyl, NR⁸R⁹-C₁-C₅-alkylcarbonyl, hydroxy-
C₁-C₅-alkyl, R⁸R⁹-aminocarbonyl, R⁸R⁹-aminocarbonyl-
C₁-C₆-alkylcarbonyl, hydroxyaminocarbonyl, R⁸R⁹-
20 aminosulfonyl, R⁸R⁹-aminosulfon-C₁-C₆-alkyl, R⁸R⁹-
amino-C₁-C₆-alkylsulfonyl and an R⁸R⁹-amino-C₁-C₆-
alkyl group;

R⁷ is selected from the group consisting of
a arylalkyl, aryl, heteroaryl, heterocyclo, C₁-C₆-
25 alkyl, C₃-C₆-alkynyl, C₃-C₆-alkenyl, C₁-C₆-
carboxyalkyl and a C₁-C₆-hydroxyalkyl group;

R^8 and R^9 and R^{10} and R^{11} are independently selected from the group consisting of a hydrido, hydroxy, C_1 - C_6 -alkyl, C_1 - C_6 -alkanoyl, aroyl, aryl, ar- C_1 - C_6 -alkyl, heteroaryl, heteroar- C_1 - C_6 -alkyl, C_2 - C_6 -alkynyl, C_2 - C_6 -alkenyl, thiol- C_1 - C_6 -alkyl, C_1 - C_6 -alkylthio- C_1 - C_6 -alkyl, cycloalkyl, cycloalkyl- C_1 - C_6 -alkyl, heterocycloalkyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, aralkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, hydroxycarbonyl- C_1 - C_6 -alkyl, hydroxycarbonylar- C_1 - C_6 -alkyl, aminocarbonyl- C_1 - C_6 -alkyl, aryloxy- C_1 - C_6 -alkyl, heteroaryloxy- C_1 - C_6 -alkyl, arylthio- C_1 - C_6 -alkyl, heteroarylthio- C_1 - C_6 -alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro- C_1 - C_6 -alkyl, trifluoromethyl- C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, alkoxycarbonylamino- C_1 - C_6 -alkyl and an amino- C_1 - C_6 -alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1 - C_6 -alkyl, ar- C_1 - C_6 -alkyl, cycloalkyl and C_1 - C_6 -alkanoyl, or wherein R^8 and R^9 or R^{10} and R^{11} and the carbon to which they are bonded form a carbonyl group, or wherein R^8 and R^9 or R^{10} and R^{11} , or R^8 and R^{10} together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen,

oxygen, or sulfur, with the proviso that only one of R^8 and R^9 or R^{10} and R^{11} is hydroxy;

R^{12} and $R^{12'}$ are independently selected from the group consisting of a hydrido, C_1 - C_6 -alkyl, aryl, ar- C_1 - C_6 -alkyl, heteroaryl, heteroaralkyl, C_2 - C_6 -alkynyl, C_2 - C_6 -alkenyl, thiol- C_1 - C_6 -alkyl, cycloalkyl, cycloalkyl- C_1 - C_6 -alkyl, heterocycloalkyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, aryloxy- C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, hydroxycarbonyl- C_1 - C_6 -alkyl, hydroxycarbonylar- C_1 - C_6 -alkyl, aminocarbonyl- C_1 - C_6 -alkyl, aryloxy- C_1 - C_6 -alkyl, heteroaryloxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkylthio- C_1 - C_6 -alkyl, arylthio- C_1 - C_6 -alkyl, heteroarylthio- C_1 - C_6 -alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro- C_1 - C_6 -alkyl, trifluoromethyl- C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, alkoxycarbonylamino- C_1 - C_6 -alkyl and an amino- C_1 - C_6 -alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1 - C_6 -alkyl, ar- C_1 - C_6 -alkyl, cycloalkyl and C_1 - C_6 -alkanoyl;

R^{13} is selected from the group consisting of a hydrido, benzyl, phenyl, C_1 - C_6 -alkyl, C_2 - C_6 -alkynyl, C_2 - C_6 -alkenyl and a C_1 - C_6 -hydroxyalkyl group; and

R^{20} is (a) $-O-R^{21}$, wherein R^{21} is selected from the group consisting of a hydrido, C_1 - C_6 -alkyl,

aryl, ar-C₁-C₆-alkyl group and a pharmaceutically acceptable cation, (b) -NH-O-R²², wherein R²² is a selectively removable protecting group such as a 2-tetrahydropyranyl, benzyl, p-methoxybenzyl, carbonyl-
5 C₁-C₆-alkoxy, trisubstituted silyl group, an o-nitrophenyl group, and a peptide synthesis resin, wherein the trisubstituted silyl group is substituted with C₁-C₆-alkyl, aryl, or ar-C₁-C₆-alkyl or a mixture thereof, (c) -NH-O-R¹⁴, where R¹⁴ is hydrido,
10 a pharmaceutically acceptable cation or C(W)R²⁵ where W is O or S and R²⁵ is selected from the group consisting of an C₁-C₆-alkyl, aryl, C₁-C₆-alkoxy, heteroaryl-C₁-C₆-alkyl, C₃-C₈-cycloalkyl-C₁-C₆-alkyl, aryloxy, ar-C₁-C₆-alkoxy, ar-C₁-C₆-alkyl, heteroaryl
15 and amino C₁-C₆-alkyl group wherein the amino C₁-C₆-alkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an C₁-C₆-alkyl, aryl, ar-C₁-C₆-alkyl, C₃-C₈-
20 cycloalkyl-C₁-C₆-alkyl, ar-C₁-C₆-alkoxycarbonyl, C₁-C₆-alkoxycarbonyl, and C₁-C₆-alkanoyl radical, or (iii) wherein the amino C₁-C₆-alkyl nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclo or heteroaryl ring, or (d) -NR²⁶R²⁷,
25 where R²⁶ and R²⁷ are independently selected from the group consisting of a hydrido, C₁-C₆-alkyl, amino C₁-C₆-alkyl, hydroxy C₁-C₆-alkyl, aryl, ar-C₁-C₆-alkyl group, or R²⁶ and R²⁷ together with the depicted nitrogen atom form a 5- to 8-membered ring

containing zero or one additional heteroatom that is oxygen, nitrogen or sulfur.

106. The compound according to claim 105
5 wherein R^3 is the substituent G-A-R-E-Y wherein

G is an aryl or heteroaryl group;

A is selected from the group consisting of

(1) -O-;

(2) -S-;

10 (3) -NR¹⁷-;

(4) -CO-N(R¹⁷) or -N(R¹⁷)-CO-, wherein R¹⁷ is hydrogen, C₁-C₄-alkyl, or phenyl;

(5) -CO-O- or -O-CO-;

(6) -O-CO-O-;

15 (7) -HC=CH-;

(8) -NH-CO-NH-;

(9) -C≡C-;

(10) -NH-CO-O- or -O-CO-NH-;

(11) -N=N-;

20 (12) -NH-NH-; and

(13) -CS-N(R¹⁸)- or -N(R¹⁸)-CS-, wherein R¹⁸ is hydrogen C₁-C₄-alkyl, or phenyl; or

25 (14) A is absent and G is bonded directly to R;

R is a moiety selected from the group consisting of alkyl, alkoxyalkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroaralkyl, heterocycloalkylalkyl, cycloalkylalkyl,
30 cycloalkoxyalkyl, heterocycloalkoxyalkyl,

aryloxyalkyl, heteroaryloxyalkyl, arylthioalkyl, heteroarylthioalkyl, cycloalkylthioalkyl, and a heterocycloalkylthioalkyl group wherein the aryl or heteroaryl or cycloalkyl or heterocycloalkyl

5 substituent is (i) unsubstituted or (ii) substituted with one or two radicals selected from the group consisting of a halo, alkyl, perfluoroalkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, amino, alkoxycarbonylalkyl, 10 alkoxy, C₁-C₂-alkylene-dioxy, hydroxycarbonylalkyl, hydroxycarbonylalkylamino, nitro, hydroxy, hydroxyalkyl, alkanoylamino, and a alkoxycarbonyl group, and R is other than alkyl or alkoxyalkyl when A is -O- or -S-;

15 E is selected from the group consisting of

- (1) -CO(R¹⁹)- or -(R¹⁹)CO-, wherein R¹⁹ is a heterocycloalkyl, or a cycloalkyl group;
- (2) -CONH- or -HNCO-; and
- 20 (3) -CO-;
- (4) -SO₂-R¹⁹- or -R¹⁹-SO₂-;
- (5) -SO₂-;
- (6) -NH-SO₂- or -SO₂-NH-; or
- (7) E is absent and R is bonded directly 25 to Y; and

Y is absent or is selected from the group consisting of a hydrido, alkyl, alkoxy, haloalkyl, aryl, aralkyl, cycloalkyl, heteroaryl, hydroxy, aryloxy, aralkoxy, heteroaryloxy, heteroaralkyl, 30 perfluoroalkoxy, perfluoroalkylthio,

trifluoromethylalkyl, alkenyl, heterocycloalkyl,
cycloalkyl, trifluoromethyl, alkoxy carbonyl, and a
aminoalkyl group, wherein the aryl or heteroaryl or
heterocycloalkyl group is (i) unsubstituted or (ii)
5 substituted with one or two radicals independently
selected from the group consisting of an alkanoyl,
halo, nitro, aralkyl, aryl, alkoxy, and an amino
group wherein the amino nitrogen is (i) unsubstituted
or (ii) substituted with one or two groups
10 independently selected from hydrido, alkyl, and an
aralkyl group.

107. The compound according to claim 106
wherein said -G-A-R-E-Y substituent contains two to
15 four carbocyclic or heterocyclic rings.

108. The compound according to claim 107
wherein each of the two to four rings is 6-membered.

20 109. The compound according to claim 106
wherein said -G-A-R-E-Y substituent has a length that
is greater than a hexyl group and a length that is
less than that of a stearyl group.

25 110. The compound according to claim 106
wherein A is -O- or -S-.

111. The compound according to claim 106
wherein R is an aryl, heteroaryl, cycloalkyl or
30 heterocycloalkyl group.

112. The compound according to claim 106 wherein E is absent.

113. The compound according to claim 106
5 wherein Y is selected from the group consisting of hydrido, an alkyl, alkoxy, perfluoroalkoxy and a perfluoroalkylthio group.

114. The compound according to claim 105
10 wherein R¹⁴ is hydrido.

115. The compound according to claim 105 wherein W of the C(W)R²⁵ is O and R²⁵ is a C₁-C₆-alkyl, aryl, C₁-C₆-alkoxy, heteroaryl-C₁-C₆-alkyl,
15 C₃-C₈-cycloalkyl-C₁-C₆-alkyl, or aryloxy group.

116. The compound according to claim 105 wherein R³ is a single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself
20 substituted at its own 4-position when a 6-membered ring and at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of a thiophenoxy, 4-chloro-phenoxy, 3-chlorophenoxy, 4-methoxyphenoxy, 3-benzodioxol-5-yloxy, 3,4-dimethylphenoxy, 4-fluorophenoxy, 4-fluorothiophenoxy, phenoxy, 4-trifluoro-methoxyphenoxy, 4-trifluoromethylphenoxy, 4-(trifluoromethylthio)phenoxy, 4-(trifluoromethylthio)thiophenoxy, 4-chloro-3-fluorophenoxy, 4-isopropoxyphenoxy, 4-isopropylphenoxy, (2-methyl-1,3-benzothiazol-5-yl)oxy, 4-(1H-imidazol-1-yl)phenoxy,
25
30

504750-237350

4-chloro-3-methylphenoxy, 3-methyl-phenoxy, 4-ethoxyphenoxy, 3,4-difluorophenoxy, 4-chloro-3-methylphenoxy, 4-fluoro-3-chlorophenoxy, 4-(1H-1,2,4-triazol-1-yl)phenoxy, 3,5-difluorophenoxy, 3,4-dichlorophenoxy, 4-cyclopentylphenoxy, 4-bromo-3-methylphenoxy, 4-bromophenoxy, 4-methylthiophenoxy, 4-phenylphenoxy, 4-benzylphenoxy, 6-quinolinyloxy, 4-amino-3-methylphenoxy, 3-methoxyphenoxy, 5,6,7,8-tetrahydro-2-naphthalenyloxy, 3-hydroxymethylphenoxy, and a 4-benzyloxyphenoxy group.

117. The compound according to claim 105 wherein said selectively removable protecting group is selected from the group consisting of a 2-tetrahydropyranyl, benzyl, p-methoxybenzyloxy-carbonyl, benzyloxycarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkoxy-CH₂- , C₁-C₆-alkoxy-C₁-C₆-alkoxy-CH₂- and an o-nitrophenyl group.

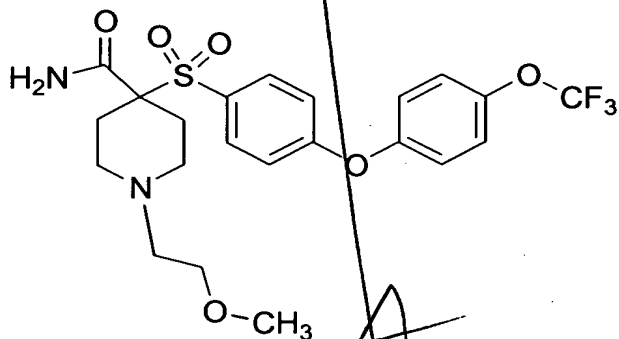
118. The compound according to claim 105 wherein said nucleophilically displaceable leaving group is selected from the group consisting of a halo, nitro, azido, phenylsulfoxido, aryloxy, C₁-C₆-alkoxy, a C₁-C₆-alkylsulfonate or arylsulfonate group and a trisubstituted ammonium group in which the three substituents are independently aryl, ar- C₁-C₆-alkyl or C₁-C₆-alkyl.

119. The compound according to claim 105 wherein g is zero.

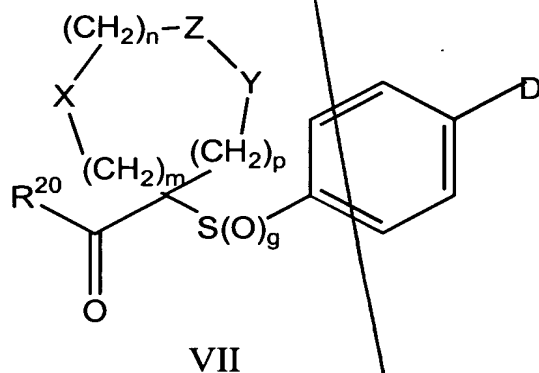
120. The compound according to claim 105 wherein R^{20} is $-NR^{26}R^{27}$.

121. The compound according to claim 120 wherein R^{26} and R^{27} are both hydrido.

122. A compound that corresponds in structure to the formula below, or a pharmaceutically acceptable salt thereof



123. An intermediate compound that corresponds in structure to formula VII, below



wherein
g is zero, 1 or 2;

D is a nucleophilically displaceable leaving group;

m is zero, 1 or 2;

n is zero, 1 or 2;

5 p is zero, 1 or 2;

the sum of $m + n + p = 1, 2, 3$ or 4;

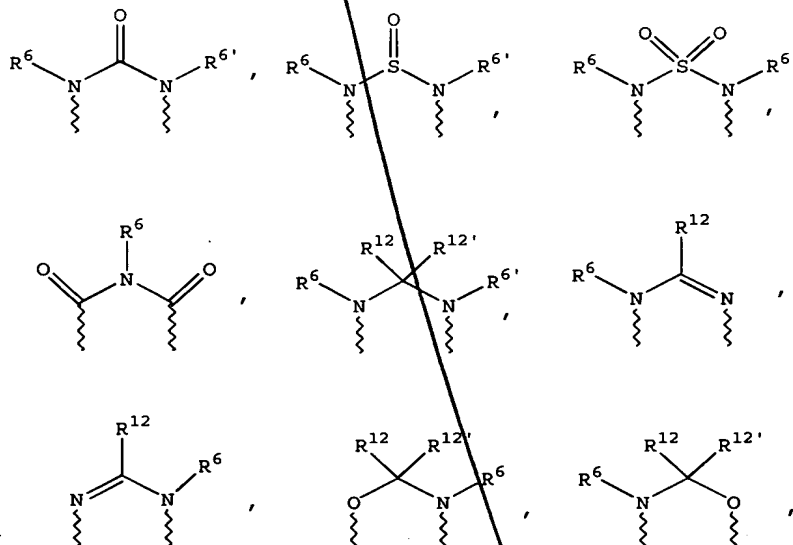
(a) one of X, Y and Z is selected from the group consisting of $C(O)$, NR^6 , O, S, $S(O)$, $S(O)_2$ and $NS(O)_2R^7$, and the remaining two of X, Y and Z are

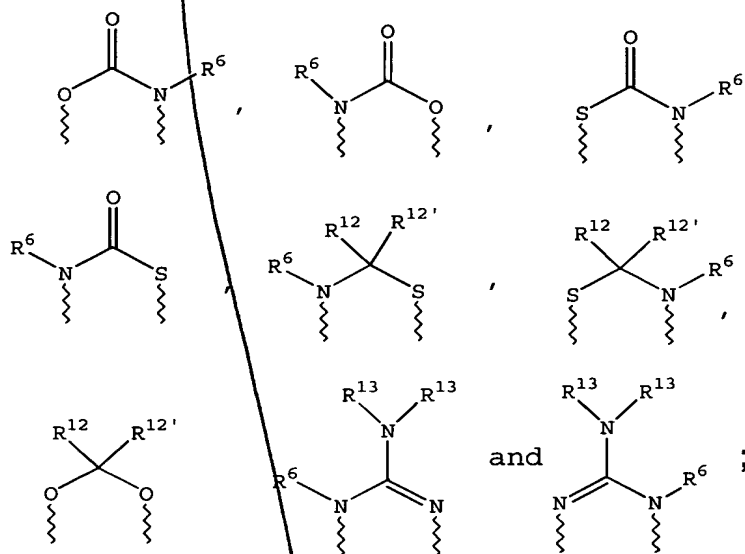
10 CR^8R^9 , and $CR^{10}R^{11}$, or

(b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of $NR^6C(O)$, $NR^6S(O)$, $NR^6S(O)_2$, NR^6S , NR^6O , SS, NR^6NR^6 and $OC(O)$, with the remaining one of X, Y and Z being CR^8R^9 , or

15 and Z being CR^8R^9 , or

(c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of





wherein wavy lines are bonds to the atoms of the depicted ring;

- 5 R^6 and $\text{R}^{6'}$ are independently selected from the group consisting of hydrido, formyl, sulfonic- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxycarbonyl- C_1 - C_6 -alkyl, hydroxycarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkylcarbonyl- C_1 - C_6 -alkyl, R^8R^9 -aminocarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxycarbonyl- C_1 - C_6 -alkylcarbonyl, hydroxycarbonyl- C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -alkylcarbonyl- C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -alkoxycarbonylcarbonyl, hydroxycarbonylcarbonyl, C_1 - C_6 -alkylcarbonylcarbonyl, R^8R^9 -aminocarbonylcarbonyl, C_1 - C_6 -alkanoyl, aryl- C_1 - C_6 -alkyl, aroyl, bis(C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl)- C_1 - C_6 -alkyl, C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_1 - C_6 -perfluoroalkyl, C_1 - C_6 -trifluoromethylalkyl, C_1 - C_6 -perfluoroalkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, heteroarycarbonyl,
- 10
- 15

heterocyclocarbonyl, C₃-C₈-heterocycloalkyl, C₃-C₈-
heterocycloalkylcarbonyl, aryl, C₅-C₆-heterocyclo,
C₅-C₆-heteroaryl, C₃-C₈-cycloalkyl-C₁-C₆-alkyl,
aryloxy-C₁-C₆-alkyl, heteroaryloxy-C₁-C₆-alkyl,
5 heteroaryl-C₁-C₆-alkoxy-C₁-C₆-alkyl, heteroarylthio-
C₁-C₆-alkyl, arylsulfonyl, C₁-C₆-alkylsulfonyl, C₅-
C₆-heteroarylsulfonyl, carboxy-C₁-C₆-alkyl, C₁-C₄-
alkoxycarbonyl-C₁-C₆-alkyl, aminocarbonyl, C₁-C₆-
alkyl(R⁸N)iminocarbonyl, aryl(R⁸N)iminocarbonyl, C₅-
10 C₆-heterocyclo(R⁸N)iminocarbonyl, arylthio-C₁-C₆-
alkyl, C₁-C₆-alkylthio-C₁-C₆-alkyl, arylthio-C₃-C₆-
alkenyl, C₁-C₄-alkylthio-C₃-C₆-alkenyl, C₅-C₆-
heteroaryl-C₁-C₆-alkyl, halo-C₁-C₆-alkanoyl, hydroxy-
C₁-C₆-alkanoyl, thiol-C₁-C₆-alkanoyl, C₃-C₆-alkenyl,
15 C₃-C₆-alkynyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₅-
alkoxycarbonyl, aryloxy-C₁-C₆-alkyl, NR⁸R⁹-
(R⁸)iminomethyl, NR⁸R⁹-C₁-C₅-alkylcarbonyl, hydroxy-
C₁-C₅-alkyl, R⁸R⁹-aminocarbonyl, R⁸R⁹-aminocarbonyl-
C₁-C₆-alkylcarbonyl, hydroxyaminocarbonyl, R⁸R⁹-
20 aminosulfonyl, R⁸R⁹-aminosulfon-C₁-C₆-alkyl, R⁸R⁹-
amino-C₁-C₆-alkylsulfonyl and an R⁸R⁹-amino-C₁-C₆-
alkyl group;

R⁷ is selected from the group consisting of
a arylalkyl, aryl, heteroaryl, heterocyclo, C₁-C₆-
25 alkyl, C₃-C₆-alkynyl, C₃-C₆-alkenyl, C₁-C₆-
carboxyalkyl and a C₁-C₆-hydroxyalkyl group;

5 R⁸ and R⁹ and R¹⁰ and R¹¹ are independently selected from the group consisting of a hydrido, hydroxy, C₁-C₆-alkyl, C₁-C₆-alkanoyl, aroyl, aryl, ar-C₁-C₆-alkyl, heteroaryl, heteroar-C₁-C₆-alkyl, C₂-C₆-alkynyl, C₂-C₆-alkenyl, thiol-C₁-C₆-alkyl, C₁-C₆-alkylthio-C₁-C₆-alkyl, cycloalkyl, cycloalkyl-C₁-C₆-alkyl, heterocycloalkyl-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, aralkoxy-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkoxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl, hydroxycarbonyl-C₁-C₆-alkyl, hydroxycarbonylar-C₁-C₆-alkyl, aminocarbonyl-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, heteroaryloxy-C₁-C₆-alkyl, arylthio-C₁-C₆-alkyl, heteroarylthio-C₁-C₆-alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro-C₁-C₆-alkyl, trifluoromethyl-C₁-C₆-alkyl, halo-C₁-C₆-alkyl, alkoxy-carbonylamino-C₁-C₆-alkyl and an amino-C₁-C₆-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C₁-C₆-alkyl, ar-C₁-C₆-alkyl, cycloalkyl and C₁-C₆-alkanoyl, or wherein R⁸ and R⁹ or R¹⁰ and R¹¹ and the carbon to which they are bonded form a carbonyl group, or wherein R⁸ and R⁹ or R¹⁰ and R¹¹, or R⁸ and R¹⁰ together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen,

oxygen, or sulfur, with the proviso that only one of R^8 and R^9 or R^{10} and R^{11} is hydroxy;

R^{12} and $R^{12'}$ are independently selected from the group consisting of a hydrido, C_1 - C_6 -alkyl, aryl, ar- C_1 - C_6 -alkyl, heteroaryl, heteroaralkyl, C_2 - C_6 -alkynyl, C_2 - C_6 -alkenyl, thiol- C_1 - C_6 -alkyl, cycloalkyl, cycloalkyl- C_1 - C_6 -alkyl, heterocycloalkyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, aryloxy- C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -alkyl, hydroxycarbonyl- C_1 - C_6 -alkyl, hydroxycarbonylar- C_1 - C_6 -alkyl, aminocarbonyl- C_1 - C_6 -alkyl, aryloxy- C_1 - C_6 -alkyl, heteroaryloxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkylthio- C_1 - C_6 -alkyl, arylthio- C_1 - C_6 -alkyl, heteroarylthio- C_1 - C_6 -alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro- C_1 - C_6 -alkyl, trifluoromethyl- C_1 - C_6 -alkyl, halo- C_1 - C_6 -alkyl, alkoxycarbonylamino- C_1 - C_6 -alkyl and an amino- C_1 - C_6 -alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1 - C_6 -alkyl, ar- C_1 - C_6 -alkyl, cycloalkyl and C_1 - C_6 -alkanoyl;

R^{13} is selected from the group consisting of a hydrido, benzyl, phenyl, C_1 - C_6 -alkyl, C_2 - C_6 -alkynyl, C_2 - C_6 -alkenyl and a C_1 - C_6 -hydroxyalkyl group; and

R^{20} is (a) $-O-R^{21}$, wherein R^{21} is selected from the group consisting of a hydrido, C_1 - C_6 -alkyl,

aryl, ar-C₁-C₆-alkyl group and a pharmaceutically acceptable cation, (b) -NH-O-R²², wherein R²² is a selectively removable protecting group such as a 2-tetrahydropyranyl, benzyl, p-methoxybenzyl, carbonyl-
5 C₁-C₆-alkoxy, trisubstituted silyl group, an o-nitrophenyl group, and a peptide synthesis resin, wherein the trisubstituted silyl group is substituted with C₁-C₆-alkyl, aryl, or ar-C₁-C₆-alkyl or a mixture thereof, (c) -NH-O-R¹⁴, where R¹⁴ is hydrido,
10 a pharmaceutically acceptable cation or C(W)R²⁵ where W is O or S and R²⁵ is selected from the group consisting of an C₁-C₆-alkyl, aryl, C₁-C₆-alkoxy, heteroaryl-C₁-C₆-alkyl, C₃-C₈-cycloalkyl-C₁-C₆-alkyl, aryloxy, ar-C₁-C₆-alkoxy, ar-C₁-C₆-alkyl, heteroaryl
15 and amino C₁-C₆-alkyl group wherein the amino C₁-C₆-alkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an C₁-C₆-alkyl, aryl, ar-C₁-C₆-alkyl, C₃-C₈-
20 cycloalkyl-C₁-C₆-alkyl, ar-C₁-C₆-alkoxycarbonyl, C₁-C₆-alkoxycarbonyl, and C₁-C₆-alkanoyl radical, or (iii) wherein the amino C₁-C₆-alkyl nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclo or heteroaryl ring, or (d) -NR²⁶R²⁷,
25 where R²⁶ and R²⁷ are independently selected from the group consisting of a hydrido, C₁-C₆-alkyl, amino C₁-C₆-alkyl, hydroxy C₁-C₆-alkyl, aryl, ar-C₁-C₆-alkyl group, or R²⁶ and R²⁷ together with the depicted nitrogen atom form a 5- to 8-membered ring containing

zero or one additional heteroatom that is oxygen, nitrogen or sulfur.

124. The compound according to claim 123
5 wherein said selectively removable protecting group is selected from the group consisting of a 2-tetrahydropyranyl, C₁-C₆-acyl, aroyl, benzyl, p-methoxybenzyloxycarbonyl, benzyloxycarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-alkoxy-CH₂-, C₁-C₆-alkoxy-
10 C₁-C₆-alkoxy-CH₂- and an o-nitrophenyl group.

125. The compound according to claim 123 wherein said nucleophilically displaceable leaving group, D, is selected from the group consisting of a
15 halo, nitro, azido, phenylsulfoxido, aryloxy, C₁-C₆-alkoxy, a C₁-C₆-alkylsulfonate or arylsulfonate group and a trisubstituted ammonium group in which the three substituents are independently aryl, ar- C₁-C₆-alkyl or C₁-C₆-alkyl.

20

126. The compound according to claim 123 wherein said halo group is fluoro.

127. The compound according to claim 123
25 wherein g is zero.

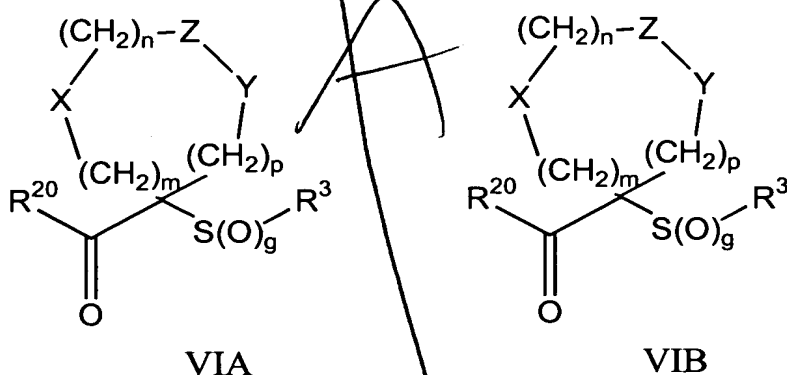
Sub B17 ~~128. A pharmaceutical composition that~~
comprises a compound according to claim 52 dissolved or dispersed in a pharmaceutically acceptable
30 carrier.

129. A pharmaceutical composition that comprises a compound according to claim 62 dissolved or dispersed in a pharmaceutically acceptable carrier.

130. A pharmaceutical composition that comprises a compound according to claim 69 dissolved or dispersed in a pharmaceutically acceptable carrier.

131. A pharmaceutical composition that comprises a compound according to claim 87 dissolved or dispersed in a pharmaceutically acceptable carrier.

132. A process for forming a metalloprotease inhibitor compound product or intermediate compound product therefore that comprises the step of coupling an intermediate compound with another moiety, wherein said intermediate compound corresponds in structure to formula VIB, below, and said product corresponds in structure to formula VIA, below:



wherein

aralkylthio, aralkylamino, heterocyclo, heteroaryl,
arylazo, hydroxycarbonylalkoxy, alkoxycarbonylalkoxy,
alkanoyl, arylcarbonyl, aralkanoyl, alkanoyloxy,
aralkanoyloxy, hydroxyalkyl, hydroxyalkoxy,
5 alkylthio, alkoxylalkylthio, alkoxycarbonyl,
aryloxyalkoxyaryl, arylthioalkylthioaryl,
aryloxyalkylthioaryl, arylthioalkoxyaryl,
hydroxycarbonylalkoxy, hydroxycarbonylalkylthio,
alkoxycarbonylalkoxy, alkoxycarbonylalkylthio, amino,

10 wherein the amino nitrogen is (i) unsubstituted,
or (ii) substituted with one or two substituents
that are independently selected from the group
consisting of an alkyl, aryl, heteroaryl,
aralkyl, cycloalkyl, aralkoxycarbonyl,
15 alkoxycarbonyl, arylcarbonyl, aralkanoyl,
heteroarylcarbonyl, heteroaralkanoyl and an
alkanoyl group, or (iii) wherein the amino
nitrogen and two substituents attached thereto
form a 5- to 8-membered heterocyclo or
20 heteroaryl ring containing zero to two
additional heteroatoms that are nitrogen, oxygen
or sulfur and which ring itself is (a)
unsubstituted or (b) substituted with one or two
groups independently selected from the group
25 consisting of an aryl, alkyl, heteroaryl,
aralkyl, heteroaralkyl, hydroxy, alkoxy,
alkanoyl, cycloalkyl, heterocycloalkyl,
alkoxycarbonyl, hydroxyalkyl, trifluoromethyl,
benzofused heterocycloalkyl, hydroxyalkoxyalkyl,
30 aralkoxycarbonyl, hydroxycarbonyl,
aryloxycarbonyl, benzofused heterocycloalkoxy,
benzofused cycloalkylcarbonyl, heterocyclo-
alkylcarbonyl, and a cycloalkylcarbonyl group,

534750-237260

carbonylamino

wherein the carbonylamino nitrogen is (i)
unsubstituted, or (ii) is the reacted amine of
an amino acid, or (iii) substituted with one or
5 two radicals selected from the group consisting
of an alkyl, hydroxyalkyl, hydroxyheteroaralkyl,
cycloalkyl, aralkyl, trifluoromethylalkyl,
heterocycloalkyl, benzofused heterocycloalkyl,
benzofused heterocycloalkyl, benzofused
10 cycloalkyl, and an N,N-dialkylsubstituted
alkylamino-alkyl group, or (iv) the carboxamido
nitrogen and two substituents bonded thereto
together form a 5- to 8-membered heterocyclo,
heteroaryl or benzofused heterocycloalkyl ring
15 that is itself unsubstituted or substituted with
one or two radicals independently selected from
the group consisting of an alkyl,
alkoxycarbonyl, nitro, heterocycloalkyl,
hydroxy, hydroxycarbonyl, aryl, aralkyl,
20 heteroaralkyl and an amino group,

wherein the amino nitrogen is
(i) unsubstituted, or (ii) substituted with
one or two substituents that are
independently selected from the group
25 consisting of alkyl, aryl, and heteroaryl,
or (iii) wherein the amino nitrogen and two
substituents attached thereto form a 5- to
8-membered heterocyclo or heteroaryl ring,
and an aminoalkyl group

30 wherein the aminoalkyl nitrogen is (i)
unsubstituted, or (ii) substituted with one or two
substituents independently selected from the group

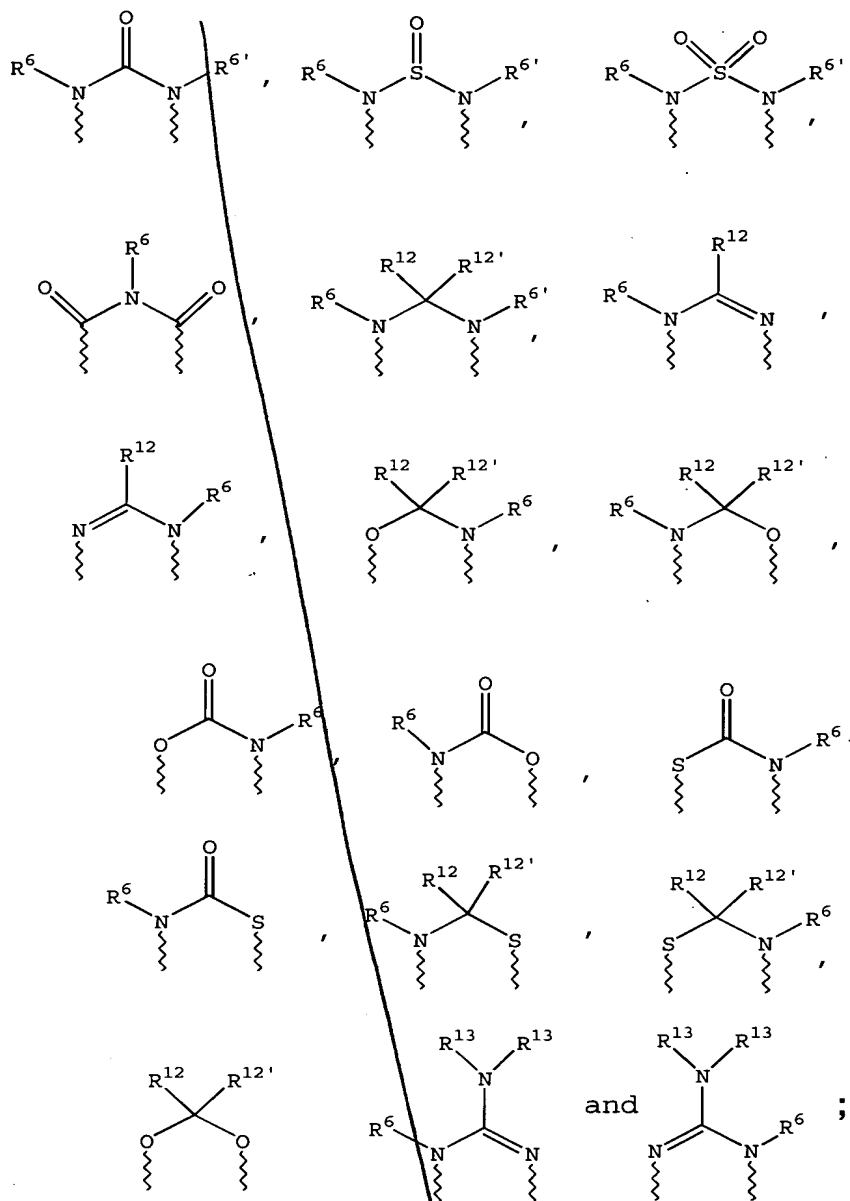
5 membered heterocyclo or heteroaryl ring;

n is zero, 1 or 2;

the sum of $m + n + p = 1, 2, 3$ or 4 ;

(b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of $\text{NR}^6\text{C}(\text{O})$, $\text{NR}^6\text{S}(\text{O})$, $\text{NR}^6\text{S}(\text{O})_2$, NR^6S , NR^6O , SS , NR^6NR^6 and $\text{OC}(\text{O})$, with the remaining one of X, Y and Z being CR^8R^9 , or

(c) n is zero and X, Y and Z together
20 constitute a moiety selected from the group
consisting of



5 wherein wavy lines are bonds to the atoms of the depicted ring;

R^6 and $R^{6'}$ are independently selected from the group consisting of hydrido, formyl, sulfonic- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxycarbonyl- C_1 - C_6 -alkyl, hydroxycarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -alkylcarbonyl- C_1 - C_6 -alkyl, R^8R^9 -aminocarbonyl- C_1 - C_6 -alkyl, C_1 - C_6 -

10

- alkoxycarbonyl-C₁-C₆-alkylcarbonyl, hydroxycarbonyl-C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonyl-C₁-C₆-alkylcarbonyl, C₁-C₆-alkoxycarbonylcarbonyl, hydroxycarbonylcarbonyl, C₁-C₆-alkylcarbonylcarbonyl,
- 5 R⁸R⁹-aminocarbonylcarbonyl, C₁-C₆-alkanoyl, aryl-C₁-C₆-alkyl, aroyl, bis(C₁-C₆-alkoxy-C₁-C₆-alkyl)-C₁-C₆-alkyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-perfluoroalkyl, C₁-C₆-trifluoromethylalkyl, C₁-C₆-perfluoroalkoxy-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-
- 10 alkyl, C₃-C₆-cycloalkyl, heteroarycarbonyl, heterocyclocarbonyl, C₃-C₈-heterocycloalkyl, C₃-C₈-heterocycloalkylcarbonyl, aryl, C₅-C₆-heterocyclo, C₅-C₆-heteroaryl, C₃-C₈-cycloalkyl-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, heteroaryloxy-C₁-C₆-alkyl,
- 15 heteroaryl-C₁-C₆-alkoxy-C₁-C₆-alkyl, heteroarylthio-C₁-C₆-alkyl, arylsulfonyl, C₁-C₆-alkylsulfonyl, C₅-C₆-heteroarylsulfonyl, carboxy-C₁-C₆-alkyl, C₁-C₄-alkoxycarbonyl-C₁-C₆-alkyl, aminocarbonyl, C₁-C₆-alkyl(R⁸N)iminocarbonyl, aryl(R⁸N)iminocarbonyl, C₅-
- 20 C₆-heterocyclo(R⁸N)iminocarbonyl, arylthio-C₁-C₆-alkyl, C₁-C₆-alkylthio-C₁-C₆-alkyl, arylthio-C₃-C₆-alkenyl, C₁-C₄-alkylthio-C₃-C₆-alkenyl, C₅-C₆-heteroaryl-C₁-C₆-alkyl, halo-C₁-C₆-alkanoyl, hydroxy-C₁-C₆-alkanoyl, thiol-C₁-C₆-alkanoyl, C₃-C₆-alkenyl,
- 25 C₃-C₆-alkynyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₅-alkoxycarbonyl, aryloxycarbonyl, NR⁸R⁹-(R⁸)iminomethyl, NR⁸R⁹-C₁-C₅-alkylcarbonyl, hydroxy-

C₁-C₅-alkyl, R⁸R⁹-aminocarbonyl, R⁸R⁹-aminocarbonyl-
C₁-C₆-alkylcarbonyl, hydroxyaminocarbonyl, R⁸R⁹-
aminosulfonyl, R⁸R⁹-aminosulfon-C₁-C₆-alkyl, R⁸R⁹-
amino-C₁-C₆-alkylsulfonyl and an R⁸R⁹-amino-C₁-C₆-
5 alkyl group;

R⁷ is selected from the group consisting of
a arylalkyl, aryl, heteroaryl, heterocyclo, C₁-C₆-
alkyl, C₃-C₆-alkynyl, C₃-C₆-alkenyl, C₁-C₆-
carboxyalkyl and a C₁-C₆-hydroxyalkyl group;

10 R⁸ and R⁹ and R¹⁰ and R¹¹ are independently
selected from the group consisting of a hydrido,
hydroxy, C₁-C₆-alkyl, C₁-C₆-alkanoyl, aroyl, aryl,
ar-C₁-C₆-alkyl, heteroaryl, heteroar-C₁-C₆-alkyl, C₂-
C₆-alkynyl, C₂-C₆-alkenyl, thiol-C₁-C₆-alkyl, C₁-C₆-
15 alkylthio-C₁-C₆-alkyl, cycloalkyl, cycloalkyl-C₁-C₆-
alkyl, heterocycloalkyl-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-
C₆-alkyl, aralkoxy-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-
alkoxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl,
hydroxycarbonyl-C₁-C₆-alkyl, hydroxycarbonylar-C₁-C₆-
20 alkyl, aminocarbonyl-C₁-C₆-alkyl, aryloxy-C₁-C₆-
alkyl, heteroaryloxy-C₁-C₆-alkyl, arylthio-C₁-C₆-
alkyl, heteroarylthio-C₁-C₆-alkyl, the sulfoxide or
sulfone of any said thio substituents, perfluoro-C₁-
C₆-alkyl, trifluoromethyl-C₁-C₆-alkyl, halo-C₁-C₆-
25 alkyl, alkoxycarbonylamino-C₁-C₆-alkyl and an amino-
C₁-C₆-alkyl group wherein the aminoalkyl nitrogen is
(i) unsubstituted or (ii) substituted with one or two

radicals independently selected from the group consisting of C₁-C₆-alkyl, ar-C₁-C₆-alkyl, cycloalkyl and C₁-C₆-alkanoyl, or wherein R⁸ and R⁹ or R¹⁰ and R¹¹ and the carbon to which they are bonded form a carbonyl group, or wherein R⁸ and R⁹ or R¹⁰ and R¹¹, or R⁸ and R¹⁰ together with the atoms to which they are bonded form a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclic or heteroaryl ring containing one or two heteroatoms that are nitrogen, oxygen, or sulfur, with the proviso that only one of R⁸ and R⁹ or R¹⁰ and R¹¹ is hydroxy;

R¹² and R^{12'} are independently selected from the group consisting of a hydrido, C₁-C₆-alkyl, aryl, ar-C₁-C₆-alkyl, heteroaryl, heteroaralkyl, C₂-C₆-alkynyl, C₂-C₆-alkenyl, thiol-C₁-C₆-alkyl, cycloalkyl, cycloalkyl-C₁-C₆-alkyl, heterocycloalkyl-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkoxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-alkyl, hydroxycarbonyl-C₁-C₆-alkyl, hydroxycarbonylar-C₁-C₆-alkyl, aminocarbonyl-C₁-C₆-alkyl, aryloxy-C₁-C₆-alkyl, heteroaryloxy-C₁-C₆-alkyl, C₁-C₆-alkylthio-C₁-C₆-alkyl, arylthio-C₁-C₆-alkyl, heteroarylthio-C₁-C₆-alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro-C₁-C₆-alkyl, trifluoromethyl-C₁-C₆-alkyl, halo-C₁-C₆-alkyl, alkoxycarbonylamino-C₁-C₆-alkyl and an amino-C₁-C₆-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii)

substituted with one or two radicals independently selected from the group consisting of C_1-C_6 -alkyl, ar- C_1-C_6 -alkyl, cycloalkyl and C_1-C_6 -alkanoyl;

R^{13} is selected from the group consisting of a hydrido, benzyl, phenyl, C_1-C_6 -alkyl, C_2-C_6 -alkynyl, C_2-C_6 -alkenyl and a C_1-C_6 -hydroxyalkyl group; and

R^{20} is (a) $-O-R^{21}$, wherein R^{21} is selected from the group consisting of a hydrido, C_1-C_6 -alkyl, aryl, ar- C_1-C_6 -alkyl group and a pharmaceutically acceptable cation, (b) $-NH-O-R^{22}$, wherein R^{22} is a selectively removable protecting group such as a 2-tetrahydropyranyl, benzyl, p-methoxybenzyl, carbonyl- C_1-C_6 -alkoxy, trisubstituted silyl group, an o-nitrophenyl group, and a peptide synthesis resin, wherein the trisubstituted silyl group is substituted with C_1-C_6 -alkyl, aryl, or ar- C_1-C_6 -alkyl or a mixture thereof, (c) $-NH-O-R^{14}$, where R^{14} is hydrido, a pharmaceutically acceptable cation or $C(W)R^{25}$ where W is O or S and R^{25} is selected from the group consisting of an C_1-C_6 -alkyl, aryl, C_1-C_6 -alkoxy, heteroaryl- C_1-C_6 -alkyl, C_3-C_8 -cycloalkyl- C_1-C_6 -alkyl, aryloxy, ar- C_1-C_6 -alkoxy, ar- C_1-C_6 -alkyl, heteroaryl and amino C_1-C_6 -alkyl group wherein the amino C_1-C_6 -alkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two substituents independently selected from the group consisting of an C_1-C_6 -alkyl, aryl, ar- C_1-C_6 -alkyl, C_3-C_8 -cycloalkyl- C_1-C_6 -alkyl, ar- C_1-C_6 -alkoxycarbonyl, C_1 -

C₆-alkoxycarbonyl, and C₁-C₆-alkanoyl radical, or
(iii) wherein the amino C₁-C₆-alkyl nitrogen and two
substituents attached thereto form a 5- to 8-membered
heterocyclo or heteroaryl ring, or (d) -NR²⁶R²⁷,

5 where R²⁶ and R²⁷ are independently selected from the
group consisting of a hydrido, C₁-C₆-alkyl, amino C₁-
C₆-alkyl, hydroxy C₁-C₆-alkyl, aryl, ar-C₁-C₆-alkyl
group, or R²⁶ and R²⁷ together with the depicted
nitrogen atom form a 5- to 8-membered ring containing
10 zero or one additional heteroatom that is oxygen,
nitrogen or sulfur.

133. The process according to claim 132
including the further step of recovering said
15 product.

134. The process according to claim 132
wherein R²⁰ is -NH-O-R²², wherein R²² is a
selectively removable protecting group.
20

135. The process according to claim 134
wherein said selectively removable protecting group
is selected from the group consisting of a 2-
tetrahydropyranyl, benzyl, p-
25 methoxybenzyloxycarbonyl, benzyloxycarbonyl, C₁-C₆-
alkoxycarbonyl, C₁-C₆-alkoxy-CH₂- , C₁-C₆-alkoxy-C₁-
C₆-alkoxy-CH₂- , an o-nitrophenyl group and a peptide
synthesis resin.

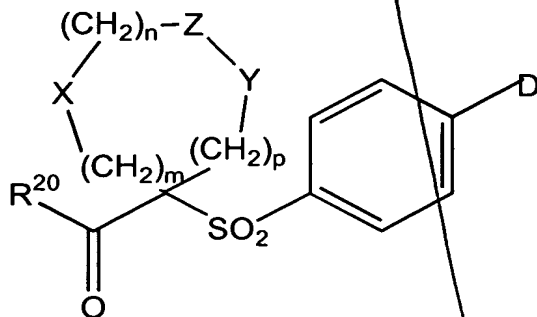
136. The process according to claim 132 wherein said coupling substituent is a nucleophilically displaceable leaving group

5 137. The process according to claim 132 wherein said nucleophilically displaceable leaving group is selected from the group consisting of a halo, nitro, azido, phenylsulfoxido, aryloxy, C₁-C₆-alkoxy, a C₁-C₆-alkylsulfonate or arylsulfonate group
10 and a trisubstituted ammonium group in which the three substituents are independently aryl, ar-C₁-C₆-alkyl or C₁-C₆-alkyl.

138. The process according to claim 132
15 wherein g is 2.

139. The process according to claim 132 wherein said R³ is an aryl or heteroaryl group.

20 140. The process according to claim 132 wherein said intermediate that corresponds in structure to formula VI corresponds in structure to formula VIIA, below,



VIIA

wherein D is said nucleophilically
displaceable leaving group and is selected from the
group consisting of a halo, nitro, azido,
phenylsulfoxido, aryloxy, C₁-C₆-alkoxy, a C₁-C₆-
5 alkylsulfonate or arylsulfonate group and a
trisubstituted ammonium group in which the three
substituents are independently aryl, ar-C₁-C₆-alkyl
or C₁-C₆-alkyl.

10 141. The process according to claim 132
including the further step of recovering said
product.

15 142. The process according to claim 132
including the further step of selectively removing
said protecting group, R²².

20 143. The process according to claim 142
wherein said protecting group, R²², is removed after
carrying out the further step of recovering said
product.

25 144. The process according to claim 143
wherein said protecting group, R²², is a
2-tetrahydropyranyl group.

30 145. The process according to claim 133
wherein R²¹ in said product after recovery is
hydrido, and including the further step of reacting
said product with hydroxyl amine or a hydroxyl amine
whose oxygen is reacted with a selectively removable

5 C₆-alkoxy-CH₂-, an o-nitrophenyl group and a peptide
synthesis resin to form a hydroxamic acid or
protected hydroxamate product.

146. The process according to claim 145
10 including the further step of recovering the product
formed.

add 13¹⁸